

University of Arkansas, Fayetteville

**ScholarWorks@UARK**

---

Theses and Dissertations

---

5-2020

## Evaluation of anthelmintic therapies in a fall calving beef cowherd

Laine Zammit

*University of Arkansas, Fayetteville*

Follow this and additional works at: <https://scholarworks.uark.edu/etd>



Part of the [Animal Diseases Commons](#), [Animal Experimentation and Research Commons](#), [Animal Sciences Commons](#), [Large or Food Animal and Equine Medicine Commons](#), and the [Parasitology Commons](#)

---

### Citation

Zammit, L. (2020). Evaluation of anthelmintic therapies in a fall calving beef cowherd. *Theses and Dissertations* Retrieved from <https://scholarworks.uark.edu/etd/3689>

This Thesis is brought to you for free and open access by ScholarWorks@UARK. It has been accepted for inclusion in Theses and Dissertations by an authorized administrator of ScholarWorks@UARK. For more information, please contact [ccmiddle@uark.edu](mailto:ccmiddle@uark.edu).

Evaluation of anthelmintic therapies in a fall calving beef cowherd

A thesis submitted in partial fulfillment  
of the requirements for the degree of  
Master of Sciences in Animal Sciences

by

Laine Zammit  
Louisiana State University  
Bachelor of Science in Animal Sciences, 2017

May 2020  
University of Arkansas

This thesis is approved for recommendation to the graduate council.

---

Jeremy Powell, Ph.D.  
Thesis Director

---

Tom Yazwinski, Ph.D.  
Committee Member

---

Beth Kegley, Ph.D.  
Committee member

## ABSTRACT

Internal parasitism inevitability prompts economic loss in beef cattle production by decreasing growth performance and reproductive traits. Today, the most widely used class of anthelmintic used to treat parasitism, is the macrocyclic lactone. Many studies have conflicting results on the efficacy of macrocyclic lactones (ML) efficacy against internal parasitism. The objective of this study was to evaluate the effectiveness of moxidectin and eprinomectin, two of the MLs, on cow performance. Multiparous fall calving, crossbred beef cows ( $n = 106$ ) were allocated randomly to 1 of 3 anthelmintic treatments: 1) Negative control (**CON**), in which cows did not receive an anthelmintic, 2) Injectable moxidectin (**MOX**) and 3) Injectable extended release eprinomectin (**ERE**). Anthelminthic administration occurred on d 0, just prior to calving. Body weights (BW), body condition scores (BCS), and fecal egg counts (FEC) were obtained throughout the duration of the calving season until weaning, occurring on days: 0, 80, 162, and 217, with weaning occurring on d217. FEC were obtained, and body weights were recorded for calves on d162 and d 217. Performance data were analyzed using the MIXED procedures of SAS, and pregnancy data were analyzed using the GENMOD procedures of SAS. Significance was fixed at  $P < 0.05$  and tendencies were established from  $0.05 \leq P \leq 0.10$ . There was no effect of anthelmintic treatment on cow BW ( $P \geq 0.57$ ) or cow BCS ( $P \geq 0.22$ ) during the 217 d study; however, CON cows tended to have lower BCS ( $P = 0.08$ ) throughout the duration of the study. Cows treated with ERE had lower FEC compared to MOX and CON groups ( $P \leq 0.001$ ), as well as a tendency for improved pregnancy ( $\chi^2 = 0.0735$ ), and calving ( $\chi^2 = 0.007$ ) rates compared to the MOX treated group. Calf average daily gain ( $P = 0.23$ ) and weaning weight ( $P = 0.35$ ) was similar regarding CON, MOX, and ERE dam treatments. Calf fecal egg counts tended to differ in relation to dam treatment on d 162 ( $P = 0.08$ ) regarding CON, MOX, and ERE cow treatments.

## **AKNOWLEDGEMENTS**

I would first like to thank the University of Arkansas Animal Science department for giving me the opportunity to further my education while being extremely kind and helpful through this whole journey of grad school. I would next like to thank Toby, Pete, Jana, Ben, and all others who work out at the UA Savoy cattle units and who came out on those cold wet mornings to help work my cows for my project, your efforts did not go unnoticed. Next, I would like to thank my friends, family, and fellow grad students for constantly supporting me in all my decisions, without all of your help and guidance I would surely have lost my sanity. Further, I would like to thank Dr. Powell and Dr. Kegley for all of their wisdom and guidance not only in the aspects of research but in everyday life which I will be able to take with me into my future career. Last but not least, I would like to thank Yaz, Tucker, and Eva for explaining and re-explaining to me the important concepts and techniques of parasitology both in the lab and from literature. I really do appreciate all the time, effort, and resources that you all gave to me in order to learn and expand my knowledge into the vast world of parasitology.

## TABLE OF CONTENTS

Introduction.....	1
Literature review.....	2
Trichostrongylus spp. life cycle and characteristics.....	2
Important internal parasites of cattle.....	4
Other, less common parasites of concern in cattle.....	8
Brief history of anthelmintics and their modes of action.....	10
Anthelmintic resistance.....	12
Anthelmintics of interest.....	14
Economics of deworming beef cattle.....	20
Conclusion.....	21
References.....	22
Chapter 1 Evaluation of anthelmintic therapies in a fall calving beef cowherd.....	27
Introduction.....	27
Materials and Methods.....	28
Results.....	33
Discussion.....	38
Conclusion.....	42
References.....	43
Tables and Figures.....	45
Appendix.....	59

## LIST OF TABLES

Table 1. Bodyweight (BW) measurements of fall calving multiparous beef cows treated prior to calving with either Moxidectin or Extended Release Eprinomectin .....	45
Table 2. Body Condition Score (BCS) measurements of fall calving multiparous beef cows treated prior to calving with either Moxidectin or Extended Release Eprinomectin .....	47
Table 3. Fecal Egg Count (Geometric Means; GM) treatment $\times$ day interaction of fall calving multiparous beef cows treated prior to calving with either Moxidectin or Extended Release Eprinomectin.....	49
Table 4. Fall 2018 average calving date $\times$ dam treatment interaction of fall calving multiparous beef cows treated prior to calving in fall 2018 with either Moxidectin, or Extended Release Eprinomectin.....	50
Table 5. Subsequent (fall 2019) reproductive performance measurements of multiparous beef cows treated prior to calving in fall 2018 with either Moxidectin or Extended Release Eprinomectin.....	51
Table 6. Subsequent (fall 2019) average calving date $\times$ dam treatment interaction of cows treated prior to calving in fall 2018 with either Moxidectin or Extended Release Eprinomectin.....	54

## LIST OF FIGURES

Figure 1. Eprinomectin or Moxidectin Treatment Effect on Mean Dam BW .....	46
Figure 2. Eprinomectin or Moxidectin Treatment Effect on Mean Dam BCS.....	48
Figure 3. Eprinomectin or Moxidectin Dam Treatment Effect on Subsequent Fall 2019 Calving Rates.....	52
Figure 4. Eprinomectin or Moxidectin Dam Treatment Effect on Subsequent Fall 2019 Pregnancy Rate by Natural Breeding and Artificial Insemination.....	53
Figure 5. Eprinomectin or Moxidectin Dam Treatment Effect on Calf Birth Weight.....	55
Figure 6. Fenbendazole Treatment Effect on Calf BW 55 Days Prior to Weaning, and at Weaning .....	56
Figure 7. Fenbendazole Treatment Effect on Calf ADG 55 Days Prior to Weaning, and at Weaning .....	56
Figure 8. Control versus Treated Dam effect on Calf 205 Day Adjusted Weaning Weight.....	57
Figure 9. Eprinomectin or Moxidectin Dam Treatment Effect on Calf 205 Day Adjusted Weaning Weight.....	57
Figure 10. Fenbendazole Treatment Effect on Calf FEC 55 Days Prior to Weaning, and at Weaning.....	58
Figure 11. Eprinomectin or Moxidectin Dam Treatment Effect on D 162 Calf FEC .....	58

## **INTRODUCTION**

There is an unquestionable certainty of negative effects and financial loss associated with internal parasitism in beef cattle productivity. Losses that are inherently common to parasitism include decreases in body weight gains, milk production, reproductive rates and body condition scores. This, in combination with decreased feed intake, inhibition of nutrient utilization, metabolism disruption and declining immune status of the animal further compounds the losses endured both physically by the animal, and financially by the producer (Kunkle et al., 2013). Actions advised for negating these parasite- associated production losses include strategic pasture rotation management practices, keeping animals in a good nutritional status and the correct use of anthelmintic products, taking into account treatment timing, product selection, and administration. The objective of this study was to evaluate the efficacy of two commercially available anthelmintic products on cow and calf performance measurements in a fall calving beef herd located at the University of Arkansas Cow Calf unit in Savoy, AR.



## LITERATURE REVIEW

### ***Trichostrongylus spp.***

Trichostrongylids, more commonly known as Trichostrongyles, belong to the superfamily Trichostrongylica. The nematodes within this superfamily are known for their small mouths, slender bodies, and similar life cycles. These parasites can measure anywhere between 450-20,000 microns, which are species and stage dependent. Trichostrongyles are considered to be the most important nematodes in ruminants due to the high level of pathogenicity they can achieve within the animal. Mixed infections are the norm, so it is hard to distinguish which species cause particular symptoms, due to the shared spectrum of affects and pathogenicity. Some of the most common genera in this family that can infect cattle include: *Trichostrongylus spp.*, *Haemonchus sp.* , *Cooperia spp.* , *Ostertagia sp.* and *Nematodirus sp.* (Levine 1968; Cydectin Pour On Technical Manual,1998).

### **Trichostrongylus Life cycle**

Levine (1968) describes the life cycle of the *Trichostrongylus* type worms as being mostly the same with some variability between species. Generally, the adult worms will produce eggs that will be excreted within the feces of the animal into the environment. Depending on whether environmental conditions are conducive enough to provide suitable oxygen, water and appropriate temperature, the egg will take about a day or more before hatching a first stage rhabditiform larva (L1).

These (L1) larvae survive by feeding on bacteria and other microorganisms that are in the surrounding fecal pat for a day or more and if conditions are still favorable they will molt into a second stage larvae (L2). The L2 will continue to feed on the bacteria and other microorganisms

around them for a few days until they molt into a third stage ensheathed infective stage larvae (L3).

The total time from egg excretion within the feces into an infective L3 larvae can take as little as 6 days or as long as several weeks depending on temperatures and other microclimatic affects that can interfere with development. Once the larvae have reached the L3 stage they migrate out of the fecal pat where many crawl up vegetation or stay on the soil's uppermost surface. During this time, the ensheathed larvae can survive from days to months, utilizing food material stored in their cells. When a suitable hosts ingests the L3, the nematode will undergo exsheathment of their cuticle and will begin the parasitic phase of the life cycle in the gastrointestinal tract of the animal. At this point, depending on the species, larvae can begin exhibiting feeding behavior whether that is consuming tissue or taking blood meals from the host animal. The larvae molt twice more, once into a fourth stage larvae (L4) , and then finally into adolescent L5's , just prior to development into mature adult worms.

The adult worms will continue to remain in their designated region within the gastrointestinal tract and reproduce. The species of the nematode determines the expected time it may take to develop into a reproductively capable adult, which is termed pre-patency as well as determine the time frame in which the adult is actively reproducing within the host, otherwise known as patency. There are many factors which can influence this timeline as well, such as: season of the year, intraburden inhibition, age,sex, species, and previous infection history of the host animal.

Furthermore, nematode egg survival within the environment can also influence the epidemiological cycle of a host animal becoming infected. Evidence of microclimatic effects on development of bovine nematode eggs were observed by Rossanigo and Gruner (1994) in a study

done in central west Argentina where fecal pats were placed in three different environments (sun, shade, and the laboratory) during three seasons of the year (summer, autumn, and fall). In this study, mean temperature and fecal water content (FWC) inside the pats were measured in order to determine effect on larval rates of development.

The genera of nematode eggs used in this study included: *Haemonchus*, *Cooperia*, *Ostertagia* and *Oseophagostomum*. The rate of development of larvae was demonstrated by the number of L3, which were extracted via the Baermann procedure, per 100 eggs deposited within the fecal pats.

It was observed that 78% of the variability of development of all genera nematode eggs into L3 larvae was explained by the following three variables: the mean temperature during the total duration of development, the mean temperature during the first one-third of the duration of total development and the minimal fecal water content.

In regards to *Haemonchus* species in particular, the mean temperature value and the minimal value of FWC explained 54% of the variability for the development of L3 larvae. Whereas, the mean maximal temperature and the minimal FWC values were the two main factors that determined the development of *Cooperia* species. Overall, developmental rates were higher in pats that were located in the shade during the summer and highest in locations that experienced more sunshine during the autumn season ; whereas, the laboratory conditions yielded more variability with its results on rate of development (Rossangio and Gruner,1994).

### **Important Internal Parasites of Cattle**

#### *Cooperia spp.*

There are many different species of *Cooperia* that affect cattle, some of the most common are: *C. punctata*, *C. pectinata*, *C. surnabada* and *C. oncophora*. *Cooperia spp.* cause

gastrointestinal inflammation/damage by penetrating the small intestine mucosa and causing acute inflammation, which increases the mucus production within the intestinal tract. Some animals may present with thickened mucosa accompanied by purple colored lesions upon necropsy (Cydectin Pour On Technical Manual, 1998).

*Cooperia* is most pathogenic when it is present in young calves and causes clinical symptoms of: enteritis, diarrhea, emaciation and death. In a study by Alicata and Lynd (1961), five calves were experimentally administered 250,000 *C. punctata* larvae and five calves were left to serve as the control group in order to measure growth rates and observe other signs of infection. The resulting clinical signs of infection consisted of soft feces, intermittent or continued diarrhea, progressive emaciation, reduced feed consumption, weight loss and listlessness in infected calves.

#### *Nematodirus helvetianus*

Nematodirus, known as the thread necked worm, resides exclusively in the small intestine of young cattle. Its eggs are easily distinguishable from the other trichostrongyle type eggs, due to its larger size and football shape. In heavy infections L4 larvae and adults cause the atrophy of villi and inflammation within the intestine (Cydectin Pour On Technical Manual, 1998). This results in disruption of digestive function and negatively affects nutrient absorption. The common signs associated with an infection of *N. helvetianus* are anorexia, diarrhea, and depressed growth (Williams, 1988).

### *The HOT Complex*

Of the various nematode species that are found within the gastrointestinal tract of cattle, some of the most important are those that are known to comprise the ‘HOT’ complex. This complex includes the genera: *Haemonchus sp.*, *Ostertagia sp.*, and *Trichostrongylus spp.* (Emery, 1996).

#### *Haemonchus placei*

*Haemonchus*, commonly called the barberpole worm, draws a large amount of blood from the animal in the L4 and adult stages during its life cycle within the host animal (Cydectin Pour On Technical Manual, 1998). They are particularly known for injecting an anticoagulant into the place of attachment at the mucosal surface so that the host loses more blood, usually more than the worm can physically ingest. This explains the hemorrhagic nature of the intestines commonly found upon necropsy in the host animal. Animals infected with large numbers usually show signs of: anemia, edema, emaciation, submandibular swelling, weakness, pale mucus membranes and weight loss (Levine, 1968).

#### *Ostertagia ostertagi*

*Ostertagia*, commonly known in cattle as the brown stomach worm, is also a blood sucking nematode in all larval and adult stages of its life cycle and is considered to be the most important cattle parasite in the United States (Cydectin Pour On Technical Manual, 1998). There are three types of ostertagiasis that present in cattle, where Type 1 ostertagiasis consists of the classic disease in calves that display diarrhea and weight loss when exposed to the parasites for the first time on pasture. The ingested larvae in these calves develop to mature adults in about 21 days (Martin et al., 1957; Anderson et al., 1965).

Pre-type 2 ostertagiasis occurs when the infective larvae are picked up during the grazing season and arrest within the abomasal wall for extended periods as opposed to continued development (type 1). This arrestment is due to *Ostertagia*'s ability to sense that the environment outside the host is not suitable for larval development and/or survival. In northern climates, this occurs in the autumn and winter, and in the southern regions, it occurs in late spring and most of the summer (Cydectin Pour on Technical Manual, 1998).

Type 2 ostertagiasis is a condition that transpires when previously arrested larvae are signaled to continue their course of maturation. This occurs in the late winter and early spring in the north, and in the south it occurs during fall. During this time, a large amount of the previously arrested pre-type 2 larvae become active in the abomasal mucosa, causing immense tissue damage, inflammation, fluid loss, and hyperemia. Acute and abrupt symptoms similar to Type 1 ostertagiasis, such as diarrhea, weight loss, and subcutaneous swelling will also arise. The morbidity and mortality levels associated with this disease are largely dependent on the level of infection and magnitude of emergence of the previously arrested larvae in the type 2 disease state. (Cydectin Pour On Technical Manual, 1998; Martin et al., 1957; Anderson et al., 1965; Myers and Taylor, 1989).

### *Trichostrongylus axei*

According to Levine (1968), *T. axei* can be highly pathogenic in large numbers. Once ingested, *T. axei* larvae migrate to the abomasal mucosa where they cause lesions, which contribute to mucosa inflammation, hyperemia and sloughing of the epithelial tissue that lines the intestinal tract. Doran (1955) found infections of *T. axei* to cause weight loss, loss of appetite, watery diarrhea and in some cases resulted in the death of calves.

## **Other, Less Common Parasites of Concern in Cattle**

### *Bunostomum phlebotomum*

*Bunostomum*, also known as the cattle hookworm, enter the host by skin penetration before migrating to the host's small intestine. As described by Levine (1968), the first sign of *Bunostomum phlebotomum* infection is hives, skin irritations, and animals itching their lower legs due to larval entrance through skin penetration, when the infection is percutaneous. Animals will later become anemic and experience diarrhea due to the blood sucking nature of the adult worms within the small intestine. The intestinal mucosa will become fluid filled and may or may not be accompanied with blood. Clinical signs are mostly observed in calves, as adult animals commonly acquire immunity due to previous infections (Cydectin Pour On Technical Manual, 1998).

### *Oesophagostomum radiatum*

Commonly referred to as the nodular worm, *O. radiatum* is unlike *Bunostomum* in that the majority of the pathogenicity and intestinal destruction that the animal endures is due to the pre-patent larvae and not the actively reproductive adult worms (Cydectin Pour On Technical Manual, 1998). This nematode can infect the animal upon ingestion, or via skin penetration.

According to Andrews and Maldonado (1942) and Mayhew (1948), the 4<sup>th</sup> stage larvae become encapsulated in nodules in the mucosa within the small and large intestine. These small raised areas grow over time to form abscesses, which may be fluid filled and may contain blood. These nodules eventually cause the intestinal tract to become greatly inflamed, and with repeated infections can be severe to the animal's health. The animal may then experience upset to their normal digestive functions and present with severe diarrhea and anorexia.

### *Monezia benedini*

*Monezia* is a helminth of the family Cestoda or more commonly known as tapeworms. Pathogenicity is fairly low and usually does not cause a major concern in the health of cattle unless found in large numbers. Tapeworm infections in cattle occur by cattle ingestion of an infected free-living mite on pasture. The mite serves as an intermediate host where the larval stage of the tapeworm occurs within the mite. Once the cattle ingest the mite, the larva are released from the digested mite and attach to the mucosa of the small intestine. The tapeworm will continue a process called strobilation until it reaches full maturity. At this time, the adult tapeworm will shed eggs, or gravid proglottids from the posterior end of the tapeworm. These shed eggs are ingested by a free-living mite which commences the life cycle of a new tapeworm.

Tapeworms do not cause severe intestinal trauma in cattle. There have been some observed negative effects of tapeworm burdens in calves, including intestinal irritation, and digestion issues with resulting diarrhea and unthriftiness (Porter, 1942).

### *Coccidia*

The term coccidia is the common name used to describe the single cell protozoan parasite known as *Eimeria spp.* that is often observed in ruminant animals. These parasites are normally not a concern with grazing cattle, as they do not usually cause clinical signs of disease even in high numbers, but in some instances, as with young or stressed animals, they cause mucosal tissue destruction, erosion, and petechial hemorrhage (Jolley and Bardsley, 2006). According to Matjila and Penzhorn, (2002) the estimated annual loss that cattle ranchers endure due to coccidiosis reaches upwards of \$400 million due to reduced feed efficiency, stunted weight gain and increased likelihood of contracting other diseases.



These coccidian parasites develop in the intestinal cells of the animals, and complete an elaborate life cycle eventually resulting in the voiding of oocysts into the feces. If environmental conditions are favorable, these oocysts can survive on vegetation, water sources, and other places where animals are maintained, for extended periods of time. As stated previously, though regular infections are common they usually do not cause clinical signs due to a buildup of challenge induced immunity. The trouble with the coccidian species occurs when the immune adult animals shed fairly large numbers of oocysts on the shared vegetation with naïve calves, which have yet to endure an initial sensitizing infection. Calves that are immunologically naïve to coccidian infections can become susceptible to a serious state of disease when placed in highly contaminated areas and faced with stressful events such as: weaning, shipping, changes in feed, crowding, and concurrent infections with other parasites. Calves diagnosed with coccidiosis usually present with bloody diarrhea, dysentery, dehydration, weakness and emaciation (Jolley and Bardsley, 2006).

### **Brief history of anthelmintics and their modes of action**

In the years that preceded 1960, the anthelmintic products available were not exceptionally effective at reducing parasite burdens and in some cases were actually harmful to the health of the animal, with some containing arsenical and nicotine. Some compounds introduced in the early 1960's such as morantel tartrate were recognized for their relatively high level of efficacy against parasitic burdens in livestock, but they are either no longer produced or used. These products were referred to as the early modern anthelmintics and were soon replaced by the second generation benzimidazoles in the late 1970s and throughout the 1980s. These products were used extensively due to their welcomed high level of efficacy against gastrointestinal nematodes and lungworms while also providing some aid in tapeworm and liver

fluke control. In 1984, the latest class of deworming products were introduced, and are referred to as the endectocides meaning that they worked against both internal and external parasites, but did not have activity against liver flukes or tapeworms. The first product released from this new drug class of macrocyclic lactones is called ivermectin (Williams and Loyacano, 2001).

The three major classes of anthelmintics that are approved for use in cattle today as outlined by Edmonds et al. (2010) includes the imidazothiazoles, benzimidazoles and macrocyclic lactones. Imidazothiazoles used in cattle is limited to the drug known as levamisole. Benzimidazoles include drugs such as albendazole, fenbendazole, and oxfendazole. The macrocyclic lactones are subdivided into two groups referred to as the avermectins, which includes ivermectin, doramectin, eprinomectin , and the milbemycins represented only by moxidectin in cattle.

#### *Imidazothiazoles mode of action*

According to Vercruysse and Claerebout (2019), this class of drugs work by attaching to nicotinic acetylcholine receptors within the nematode's nerve cells, resulting in spastic paralysis. The subsequent paralysis of the nematode allows it to be expelled by the peristalsis action of the host animal.

#### *Benzimidazoles mode of action*

Benzimidazoles work against the nematodes, cestodes, and trematodes by selectively binding to the heminth's beta- tubulin molecules, thereby inhibiting microtubule production, which in turn causes the parasite to slowly die due to loss of intracellular transport mechanisms. Martin (1997). Inhibition of microtubule formation induces the disruption of cellular transport and energy metabolism, which in turn depletes energy reserves as well as disrupts the excretion of waste products. All of these processes work to disrupt the normal bodily processes of the

parasite, which in turn inhibits its ability to function properly and decreases worm survivability (Vercruysse and Claerebout, 2019).

#### *Macrocyclic lactones mode of action*

The avermectin, and milbemycin subgroups within the macrocyclic lactone class have minor differences in their molecular properties relative to parasitocidal activities, but generally both work against the nematode by increasing the opening of the glutamate gated chloride (GluCl) channels, which allows for an influx of chloride ions into nervous and muscular tissue. The influx of these chloride ions causes paralytic effects on different neuromuscular systems such as the pharynx, reproductive tract and the body wall of the parasite. The paralysis of the body wall musculature allows the parasite to be immobile, and susceptible to rapid expulsion by the host animal via peristalsis. Paralysis of the pharynx inhibits the ability of the parasite to feed which results in worm death by starvation (Vercruysse and Claerebout, 2019).

#### **Anthelmintic resistance**

Over the past few decades there has been an observed decrease in the efficacy of anthelmintics due to an increased resistance by the nematodes to the anthelmintic drugs we rely on in order to protect our cattle from parasitic infections. Resistance is said to be present when the frequency of the individuals within a parasite population that would normally be affected by a dose or the concentration of a compound are no longer affected by that dose or concentration and require a greater amount for a certain level of efficacy (Wolstenhome et al., 2004). Resistance is generally confirmed when there is less than 90% reduction in geometric mean worm count population after treatment administration. (Taylor et al., 2002)

Additionally, it has been reported that multidrug resistance for many species of parasites has also become a common (Mejia et al., 2003) and that it can be assumed that once resistance is

observed for one anthelmintic in a class, that there is also some level of resistance to other drugs in the same class as well (Wolstenhome et al., 2004). Partial contribution to the increased resistance can be attributed to the fact that many producers strictly rely on drug administration for worm control, while neglecting husbandry and managerial options such as good pasture management practices in order to reduce contamination, maintaining refugia in a herd. (Gasbarre et al., 2009; Kaplan and Vidyashankar, 2012; Demeler et al., 2010). Resistance is not confined to the United States, but has become a worldwide concern as resistance has been observed in the UK, New Zealand, Argentina, and Brazil (Coles, 2002 ; Soutello et al., 2007; Suarez and Cristel , 2007 ; Kaplan and Vidyashankar , 2012 ; Gasbarre et al., 2009 ; Anziani et al., 2004 ; Chaudhry et al., 2014).

*Cooperia* species are perhaps the most often cited as being resistant to the avermectin drug class. Due to their observed abundance and ability to achieve pathogenic populations in young cattle, *Cooperia* infections in calves cause high levels of morbidity and subsequent mortality that is not curbed with routine anthelmintic intervention (Edmonds et al., 2010; Fiel et al., 2001; Anziani et al., 2001; Mejia et al., 2003).

In one study, Edmonds et al. (2010) used 50 yearling heifers with a known history of harboring anthelmintic resistance nematodes. They were treated with either: injectable ivermectin, injectable moxidectin, oral fenbendazole, oral oxfendazole, or injectable saline control. Upon necropsy, the results of the trial showed that fenbendazole and oxfendazole efficacy against *Cooperia* spp. was greater than 95% while moxidectin resulted in 88% parasite reduction and ivermectin treated heifers resulted in no reduction in adult *Cooperia* spp. These results show that neither moxidectin or ivermectin were efficacious ( > 90% efficacy) against

adult *Cooperia* spp., specifically *Cooperia oncophora*; further demonstrating the resistance and dose limiting nature of this species against all drugs of the macrocyclic lactone class.

### **Anthelmintics of Interest**

#### *Moxidectin*

As mentioned previously, moxidectin falls into the subclass milbemycin, which is included in the family of anthelmintics known as the macrocyclic lactones. According to Vercruysse and Claerebout, (2019) these products are well absorbed when administered orally and by way of injection whereas when used in formulation as a pour on, the substance has a more variable absorption within the animal. This particular anthelmintic concentrates within the adipose tissue of the animal upon administration, which accounts for its ability to sustain concentrations that allow it to be actively effective against parasites over an extended period of time.

#### *Performance of cattle treated with Moxidectin*

There have been various studies constructed in order to determine the efficacy of moxidectin (MOX) as an anthelmintic product when used in cattle (Whang et al.1994 ; Reinmeyer and Cleale, 2002 ; Maritorena-Diez et al., 2005 ; Ives et al.,2007;Walker et al., 2013; Yazwinski et al.,2013 ; Powell et al.,2008; Cleale et al., 2004). Moxidectin treated cattle have been observed to have an increase body weight (Walker et al., 2013; Whang et al., 1994) and increased average daily gain (Cleale et al., 2004; Powell et al., 2008) as compared to controls. A study conducted by Yazwinski et al. in 2006, observed significant improvements for average daily gains in cattle receiving MOX injections at multiple dose rates as compared to those control animals in a combination of three studies which took place in 3 different geographical locations: Arkansas, Louisiana, and Wisconsin. Regardless of the study location, post-treatment

interval or the dose rate of moxidectin, a 33% increase in average daily gain in cattle was observed in treated cattle compared to those that were in the control groups.

#### *Moxidectin effect on fecal egg count reduction*

Along with performance data there have been studies that have observed the effects on fecal egg count reductions in Moxidectin treated cattle when compared to other macrocyclic lactones (Soutello et al., 2010; Ives et al., 2007; Yazwinski et al., 2013) as well as compared to control animals (Maritorena-Diez et al., 2005; Cleale et al., 2004; Whang et al., 1994; Powell et al., 2008). In one study reported by Yazwinski et al. (2013), 24 study calves that were believed to have had no prior anthelmintic treatment were blocked into 4 treatment groups: control, topical ivermectin, topical moxidectin and injectable moxidectin. Two weeks after treatment administration a fecal egg count reduction test showed a 93% fecal nematode reduction with injectable moxidectin and upon necropsy (15-18 days post treatment) the topical formulation of moxidectin resulted in (>90%) efficacy against all common nematodes for cattle.

#### *Eprinomectin extended release formulation*

Eprinomectin is a semi-synthetic compound of the avermectin sub group that was originally formulated for topical administration for the use of nematode, insect, and mite control in cattle. Due to its capacity to be reformulated into a unique micelle matrix it was formulated as such and evaluated as well as marketed as an anthelmintic that would extend the therapeutic effectiveness in treated animals for prolonged period of time of about 120 days. (Soll et. al, 2013).

One of the driving forces behind the popularity of this extended release product was the convenience factor for cattle producers. The ability for a single product administration for season long control of parasites requires less handling, therefore less stress to the animals. The extended

release formulation consists of a 5% sterile solution of eprinomectin incorporated in a poly (D, L-lactide-co-glycolic) acid (PGLA) polymer matrix. Following subcutaneous injection at a dose of 1.0 mg/kg BW, eprinomectin is released from the PGLA matrix at injection site. The eprinomectin plasma concentrations remain therapeutic for approximately 100 days post treatment, with an augmenting additional spike at day 70 post treatment. After this second spike, there is a gradual decline of plasma eprinomectin concentration until approximately day 150 post-original administration. This unique technology of an extended release confers extended nematode control anywhere from 100-150 days after a single administration (Forbes, 2013).

#### *Performance of cattle treated with Eprinomectin*

Eprinomectin has been observed to improve performance parameters of cattle treated with extended release formulation as opposed to those that were treated with injectable ivermectin (Andresen et al., 2018) as well as when compared to control animals (Rehbein et al., 2013).

A study by Andresen et al. (2018), used two experiments to determine performance and reproductive success of a fall calving beef herd of cows that were treated with either extended release eprinomectin or conventional injectable ivermectin. In the first experiment, 119 fall calving cows were assigned to either a treatment of injectable ivermectin (n=53, CONV) or injectable extended release eprinomectin (n=66, EPR). The performance results of the study showed that cows treated with EPR observed not only a greater average daily gain, but also a greater change in body weight ( $P \leq 0.01$ ) compared to CONV treated cows. The reproductive performances observed in the study presented a tendency for higher pregnancy rates in cattle that were administered EPR as opposed to those in the CONV treatment group ( $P = 0.15$ ). In addition to this tendency, it was also observed that the calves of the EPR treated cows had greater

weaning weights, even at a younger age compared to those calves from the CONV treated cows ( $P \leq 0.01$ ).

In the second experiment in this study, 74 yearling fall replacement heifers were similarly placed in treatment groups represented by the first experiment (n=33; CONV) or (n=44; EPR). The performance evaluation showed that EPR treated heifers attained heavier body weights ( $P \leq 0.10$ ), a greater weight gain ( $P \leq 0.01$ ), and greater daily gain ( $P \leq 0.01$ ) compared to those heifers administered the CONV treatment. The reproductive performance data in regards to the heifer treatment groups also revealed that EPR treated heifers overall pregnancy rates were greater (95%) compared to CONV treated heifers (73%).

#### *Eprinomectin effect on fecal egg count reduction*

There have been many studies over the years that have demonstrated a high therapeutic efficiency and acceptability of extended release eprinomectin (EPR) when used in cattle to treat multiple species of gastrointestinal and pulmonary nematodes, including those that are inhibited within the host (Hunter et al., 2013; Rehbein et al., 2013; Soll et al., 2013; Rehbein et al., 2013). In addition to a record of high therapeutic efficiency against nematode infections, EPR has also been demonstrated to confer anthelmintic activity for extended periods of time ranging anywhere from 100-150 days post treatment depending on the species of nematode (Soll et al., 2013; Rehbein et al., 2013).

A total of 10 studies were used collectively in order to observe the duration of efficacy in different breeds of cattle in different geographical areas wherein the cattle were challenged with nematode infections from 100- 150 days following treatment with EPR. Of the 10 studies, 5 took place in the U.S., 1 took place in the U.K. and 4 took place in Germany. Study 1 and 2 were created to evaluate efficacy of extended release injectable eprinomectin (EPRI) against nematode



infections in cattle for 100 to 120 days after treatment, studies 3-8 were created to evaluate efficacy after 120 days post treatment, and studies 9 and 10 were created to evaluate efficacy after 150 days post treatment. All studies were conducted by randomized block design based on pretreatment body weights.

Cattle used to test the efficacy of EPRI against a single challenge of infective stage gastrointestinal nematodes at 100 days post treatment exhibited an overall nematode reduction of >99%. Treated cattle had fewer ( $P < 0.01$ ) nematodes of the species: *C. oncophora*, *C. surnabada*, *C. punctata* and *T. axei* as compared to those animals that were treated with control saline injections.

Cattle used to test the efficacy of EPRI against a single challenge of infective stage gastrointestinal nematodes and/or lungworms after 120 days post treatment were shown to exhibit an overall nematode reduction of  $\geq 92\%$ . These treated cattle also had significantly fewer ( $P < 0.05$ ) of the following species: *H. contortus*, *O. lyrata*, *O. ostertagi*, *O. leptospicularis*, *O. circumcincta*, *O. trifurcata*, *T. axei*, *C. punctata*, *B. phlebotomum* and *O. radiatum*, as compared to the control cattle injected with saline.

Lastly, cattle used to test the efficacy of (EPRI) against a single challenge of infective stage nematodes at 150 days post treatment were shown to have an overall nematode reduction of  $\geq 92\%$ . These EPRI treated cattle harbored significantly fewer nematodes ( $P < 0.01$ ) of the species: *H. contortus*, *B. phlebotomum*, *O. radiatum*, when compared to cattle that were treated with the saline injection, serving as a control. Therefore, these studies confirmed the high efficacy of the extended release eprinomectin formulation against nematode challenge at 100, 120, and 150 days following treatment (Soll et al., 2013; Rehbein et al., 2013).

### *Fenbendazole*

Fenbendazole is a broad spectrum anthelmintic that falls in the benzimidazole drug class and is most commonly used to treat nematode infections in livestock. It is available in various formulations such as a bolus, suspension, or paste. It is most commonly administered orally due to its lack of water solubility, and the ability of the compound to transfer to the parasite by transcuticular diffusion after absorption through the gastrointestinal tract. (Vercruysse and Claerebout, 2019; Enejoh and Suleiman, 2017).

### *Performance of cattle treated with Fenbendazole*

In a study conducted by Troxel et al., (1993) fenbendazole (FEN) was administered to cows in an oral suspension at the rate of 5 mg/kg of body weight, 45 to 60 days prior to calving. Though the calves born from treated dams had a resulting 15.3 percent increase in ADG compared to calves born from untreated dams, the observed differences were not deemed significant.

The results of a two year study conducted by Stromberg et al., (1997) further supports the idea that cows treated with FEN have increased reproductive performance when compared to control cows and that calves treated with FEN significantly outgained non-treated control calves. In the first year of this study, 60 cows and 12 bred heifers were stratified and randomly allocated to either treated or control groups. Similarly, in the second year of the study, 61 cows and 4 bred heifers were used in order to compare variances over the successive two years. Cows receiving anthelmintic treatments were administered an oral fenbendazole suspension at the dose rate of 5 mg/kg of bodyweight just prior to turnout on spring pasture. Control cows did not receive an anthelmintic treatment. Cows and calves in the treatment groups were administered an oral fenbendazole suspension at the dose rate of 5 mg/kg of bodyweight at midsummer when moved

to fresh pastures. Both groups grazed on similar but separate pastures for the duration of the study. The results of the study had shown an increase ( $P = 0.0357$ ) in reproductive performance in the FEN treated cows over the course of the two-year study with an 11.8% and 12.4 % increased pregnancy rate as compared to the control groups in years 1 and 2 of the study. It was also observed that the FEN treated calves had an increased average daily gain of 0.13 kg compared to control calves as well as FEN treated calves weaning at 18.5 kg heavier compared to those control calves ( $P = 0.0001$ ).

#### *Fenbendazole effect on fecal egg count reduction*

As evidenced by the previously mentioned study by Troxel et al., (1993) FEN was shown to indirectly decrease fecal egg counts at 90 days of age in calves that were born to cows treated with FEN prior to calving as compared to those calves born from cows that were left untreated.

Furthermore, Stromberg et al., (1997) observed that FEN treated cows and calves not only experienced increased performance compared to control animals but also exhibited lower fecal egg counts throughout the study as well. In his work, control cows experienced higher fecal egg counts in the collections that occurred in July ( $P < 0.0001$ ) and October ( $P = 0.0083$ ) as compared to the FEN treated cows during the study. The study also reported that calves treated with FEN had lower fecal egg counts ( $P < 0.0001$ ) during the October collection at weaning as compared to control calves.

#### **Economics on deworming beef cattle**

In a study using six regional cow- calf operation budgets, Lawrence and Ibarburu (2007) evaluated the estimated costs of eliminating pharmaceutical products on calf weaning rate and the subsequent production costs. Of the pharmaceutical technologies investigated in this study, de-wormer technology had the most significant impact on calf weaning rate, with an expected

value of 23.6%, which leads to improved weaning rates. It should be noted that weaning rate includes both pregnancy rate and survival rate of the calf. Also, there was an observed 34% expected impact on a break even selling price when removing anthelmintic products within a beef cow calf operation, that correlated to an added cost to the producer of \$165.47 per head.

These findings are crucial in understanding the negative impacts that can occur when withholding anthelmintic treatment, and further convey the importance for continuing research of anthelmintic efficacy in different beef production systems.

## **Conclusion**

Gastrointestinal nematode infections in cattle have negative impacts on cattle health and productivity. Proper deworming protocols and fecal egg count reduction tests can be useful in mitigating these production losses and negative effects on cattle performance when dealing with parasitic infections.

As stated by Troxel et al., (1993), deworming programs have to take into account the costs and returns of deworming. Costs may include: the anthelmintic product, equipment, labor, and the gathering cattle and the returns may include: dam reproduction rates, cutting added production costs of supplemental feeding products and increased weaning weights in calves. Producers can properly use commercially available anthelmintic products such as moxidectin, extended release eprinomectin and fenbendazole as an important tool in order to implement effective management strategies that are conducive to combating the negative effects of gastrointestinal nematode infections in their beef cattle herd.

## REFERENCES

- Alicata, J.E., & Lynd, F.T. (1961). Growth rate and other signs of infection in calves experimentally infected with *Cooperia punctata*. *Am. J. Vet. Res.*, 22, 704-70.
- Anderson, N.J., Armour, J., Jarret, W.F. H., Jennings, F.W., Ritchie, J.S.D., & Urquhart, G.M. (1965). A field study of parasitic gastritis in cattle. *Vet. Rec.*, 77, 1196-1204.
- Andresen, C. D., Loy, D.D., Brick, T.A., & Gunn, P.J. (2018). Case Study: Effects of extended release eprinomectin on cow-calf performance and reproductive success in a fall calving beef herd. *Prof. Anim. Sci.*, 34, 223-229.
- Andrews, J.S., & Maldonado, J.F. (1942) Intestinal pathology in experimental bovine esophagostomiasis. *Am.J.Vet.Res.*, 3, 17-27.
- Anziani, O.S., Zimmerman, G., Guglielmone, A.A., Vazquez, R., & Suarez, V. (2001). Avermectin resistance in *Cooperia pectinata* in cattle in Argentina. *Vet.Rec.*, 149, 58-59.
- Anziani, O. S., Suarez, V., Guglielmone, A.A., Warnke, O., & Coles, G.C. (2004). Resistance to benzimidazole and macrocyclic lactone anthelmintics in cattle nematodes in Argentina. *Vet. Parasitol.*, 122, 303-306.
- Chaudhry, U., Miller, M., Yazwinski, T., Kaplan, R., & Gilleard, J. (2014). The presence of benzimidazole resistance mutations in *Haemonchus placei* from US cattle. *Vet. Parasitol.*, 204, 411-415.
- Cleale, R..M., Hart, K.B., Hutchens, D.E., Johnson, E.G., Paul, A.J., Smith, L.L., Tucker, C., Yazwinski, T., Doscher, M.E., Grubbs, S.T., Wulster-Radcliffe, M., & Amodie, D.M. (2004). Effects of subcutaneous injections of a long acting moxidectin formulation in grazing beef cattle on parasite fecal egg reduction and animal weight gain. *Vet. Parasitol.*, 126, 325-338.
- Coles, G.C. (2002). Cattle nematodes resistant to anthelmintics: why so few cases? *Vet. Res.*, 33, 481-489.
- Cydectin Pour-On Technical Manual. (1998). Fort Dodge.
- Demeler, J., Küttler, U., & von Samson-Himmelstjerna, G. (2010). Adaptation and evaluation of three different in vitro tests for the detection of resistance to anthelmintics in gastrointestinal nematodes of cattle. *Vet. Parasitol.*, 170, 61-70.
- Doran, D.J. (1955) The course of infection and pathogenic effect of *Trichostrongylus axei* in calves. *Am. J.Vet.Res.*, 16, 401-40.

- Edmonds, M.D., Johnson, E.G., & Edmonds, J.D. (2010). Anthelmintic resistance of *Ostertagia ostertagi* and *Cooperia oncophora* to macrocyclic lactones in cattle from the western United States. *Vet. Parasitol.*, 170, 224-229.
- Emery, D.L. (1996) Vaccination against worm parasites of animals. *Vet. Parasitol.*, 64, 31-45.
- Enejoh, O.S., and Suleiman, M.M. (2017) Anthelmintics and their application in veterinary medicine. *Res. in Med. & Eng. Sci.*, 2, n.p.
- Fiel, C. A., Saumell, C.A., Steffan, P.E., & Rodriguez, E.M. (2001). Resistance of *Cooperia* to ivermectin treatments in grazing cattle of the Humid Pampa, Argentina. *Vet. Parasitol.*, 97, 211-217.
- Forbes, A.B. (2013). LongRange(eprinomectin 5%) extended-release injection parasiticide and the utility of extended-activity antiparasitics in cattle. *Vet. Parasitol.*, 192, 308-312.
- Gasbarre, L.C., Smith, L.L., Lichtenfels, J.R., & Pilitt, P.A. (2009). The identification of cattle nematode parasites resistant to multiple classes of anthelmintics in a commercial cattle population in the US. *Vet. Parsitol.*, 166, 281-285.
- Hunter III, J. S., Yoon, S., Yazwinski, T.A., Williams, J.C., & Rehbein S. (2013). The efficacy of eprinomectin extended-release injection against naturally acquired nematode parasites of cattle. with special regard to inhibited fourth- stage *Ostertagia* larvae. *Vet. Parasitol.*, 192, 346-352.
- Ives, S. E., Yazwinski, T.A., & Tucker, C.A. (2007). Fecal egg count recuctions and performance effect of dectomax, cydectin, and cydectin plus synanthic as used in feedlot steers. *Vet. Ther.*, 8, 311-317.
- Jolley, W. R., & Bardsley, K.D. (2006). Ruminant Coccidiosis. *Vet. Clin. Food Anim.*, 22, 613-621.
- Kaplan, R. M., & Vidyashankar, A.N. (2012). An inconvenient truth: Global warming and anthelmintic resistance. *Vet. Parasitol.*, 186, 70-78.
- Kunkle, B.N., Williams, J.C., Johnson, E.G., Stromberg, B.E., Yazwinski, T.A., Smith, L.L., Yoon, S., & Cramer, L.G. (2013). Persistant efficacy and production benefits following use of extended-release injectable eprinomectin in grazing beef cattle under field conditions. *Vet. Parasitol.*, 192, 332-337.
- Lawrence, J. D., & Ibarburu, M.A. (2007). Economic analysis of pharmaceutical technologies in modern beef production. Conference on Applied Commodity Price Analysis, Forecasting, and Market Risk Management. Chicago: Iowa State University.
- Levine, N. D. (1968). *Nematode Parasites of Domestic Animals and of Man*. Urbana, Illinois: Burgess Publishing Company.

- Maritorena-Diez, S., Roa-Vásquez, S., Marín-Mejía, B., Alonso-Díaz, M.A., & Rodríguez-Vivas, R.I. (2005). Efficacy of moxidectin 0.5% pour-on against naturally acquired nematode infections in cattle in the Mexican tropics. *Vet. Parasitol.*, 134, 117-120.
- Martin, R. (1997). Modes of Action of Anthelmintic Drugs. *Vet. J.*, 154, 11-34.
- Martin, W.B., Thomas, B.A.C., & Urquhart, G.M. (1957) Chronic diarrhea in housed cattle due to atypical parasitic gastritis. *Vet. Rec.*, 69: 736-739.
- Matjila, P.T., & Penzhorn, B.L. (2002). Occurrence and diversity of bovine coccidian at three localities in South Africa. *Vet. Parasitol.*, 104, 93-102
- Mayhew, R.L. (1948) Studies on bovine gastrointestinal parasites. X. The effects of nodular worm *Oesophagostomum* on calves during the prepatent period. *Am. J. Vet. Res.* 9, 30-34.
- Mejia, M.E., Fernández-Igartúa, B.M., Schmidt, E.E. & Cabaret J. (2003). Multispecies and multiple anthelmintic resistance on cattle nematodes in a farm in Argentina: the beginning of high resistance? *Vet. Res.*, 34, 461-467.
- Myers, G.H., and Taylor, R.F. (1989) Ostertagiasis in cattle. *J Vet. Diagn. Invest.*, 1, 195- 200.
- Porter, D. A. (1942). Tapeworms and Roundworm Parasites of Cattle. In U. S. Agriculture., *Keeping Livestock Healthy-Yearbook of Agriculture* (pp. 593-604). Washington, D.C.: United States Government Printing Office.
- Powell, J. G., Yazwinski, T.A., Tucker, C.A., Johnson, Z.B., Reynolds, J.J., Brown, A.H., Hornsby, J.A., & Prewett, C. (2008). *Evaluation of long-acting moxidectin and ivermectin in the development of replacement beef heifers*. University of Arkansas Division of Agriculture, Department of Animal Science. Fayetteville: Arkansas Agricultural Experiment Station.
- Rehbein, S., Baggott, D.G., Johnson, E.G., Kunkle, B.N., Yazwinski, T.A., Yoon, S., Cramer, L.G., and Soll, M.D. (2013). Nematode burdens of pastured cattle treated once at turnout with eprinomectin extended- release injection. *Vet. Parasitol.*, 192, 321-331.
- Rehbein, S., Baggott, D.G., Royer, G.C., Yoon, S., Cramer, L.G., & Soll, M.D. (2013). Therapeutic efficacy of eprinomectin extended- release injection against induced infections of developing (fourth-stage larvae) and adult nematode parasites of cattle. *Vet. Parasitol.*, 192, 313-320.
- Reinemeyer, C. R., & Cleale, R.M. (2002). Dose confirmation of moxidectin 1% non-aqueous injectable and moxidectin 0.5% pour-on formulations against experimentally induced infections of larval and adult stage *Oesophagostomum radiatum* and *Trichuris discolor* in cattle. *Vet. Parsitol.*, 108, 75-83.

- Rossanigo, C. E., & Gruner, L. (1994). Relative effect of temperature and moisture on the development of strongyle eggs to infective larvae in bovine pats in Argentina. *Vet. Parasitol.*, 55, 317-325.
- Soll, M. D., Kunkle, B.N., Royer, G.C., Yazwinski, T.A., Baggott, D.G., Wehner, T.A., Yoon, S., Cramer, L.G., & Rehbein, S. (2013). An eprinomectin extended-release injection formulation providing nematode control in cattle for up to 150 days. *Vet. Parasitol.*, 192, 313-320.
- Soutello, R.G.V., Dourado- Coelho, W.M., Paes de Oliveira, F., Francisco-Fonzar, J., Luquetti, B.C., Pereira de Souza, R.F., Zocoller- Seno, M.C., & Talamini do Amarante, A.F. (2010). Evaluation of reduction in egg shedding of gastrointestinal nematodes in cattle following administration of anthelmintics. *Rev. Bras. Parasitol. Vet.*, 19, 183-185.
- Soutello, R.G.V., Seno, M.C.Z., & Amarante, A.F.T. (2007). Anthelmintic resistance in cattle nematodes in northwestern São Paulo State, Brazil. *Vet. Parasitol.*, 148, 360-364.
- Stromberg, B.E., Vathauer, R.J., Schlotthauer, J.C., Myers, G.H., Haggard, D.L., King, V.L., & Hanke, H. (1997) Production responses following strategic parasite control in a beef cow/calf herd. *Vet. Parasitol.*, 68, 315-322.
- Suarez, V. H., & Cristel, S.L. (2007). Anthelmintic resistance in cattle in western Pampeana Region of Argentina. *Vet. Parasitol.*, 144, 111-117.
- Taylor, M.A., Hunt, K.R., and Goodyear, K.L. (2002) Anthelmintic resistance detection methods. *Vet. Parasitol.*, 103, 183- 194
- Troxel, T. R., Clark, M.B., Gasch, C.L., Boyd, L.J., & Essig, H.W. (1993). Effect of fenbendazole on nematode parasites and on preweaning average daily gain in beef cow herds. *Prof. Anim. Sci.*, 9, 45-52.
- Vercruysse, J. E. & Claerebout E. *Mechanisms of Action of Anthelmintics*. Merk Manual - Veterinary Manual:  
<https://www.merkvetmanual.com/pharmacology/anthelmintics/mechanisms-of-action-of-anthelmintics> (Accessed on June 12, 2019).
- Walker, R.S., Miller, J.E., Monlezun, C.J., LaMay, D., Navarre, C., & Ensley, D. (2013). Gastrointestinal nematode infection and performance of weaned stocker calves in response to anthelmintic control strategies. *Vet. Parasitol.*, 197, 152-159.
- Whang, E. M., Bauer, C., Kollmann, D., & Bürger, H.J. (1994). Efficacy of two formulations ('injectable' and 'pour on') of moxidectin against gastrointestinal nematode infections in grazing cattle. *Vet. Parsitol.*, 51, 271-281.
- Williams, J. (1988). *Internal Parasites of Cattle*. Somerville, NJ, U.S.A.: Hoechst-Roussel Agri-Vet Company.



- Williams, J.C., & Loyacano, A.F. (2001). Internal parasites of cattle in Louisiana and other southern states. LSU AgCenter Research and Extension.
- Wolstenhome, A. J., Fairweather, I., Prichard, R., von Samson-Himmelstjerna, G., & Sangster, N.C. (2004). Drug resistance in veterinary helminths. *Trends Parasitol.*, 20, 469-476.
- Yazwinski, T. A., Tucker, C.A., Wray, E., Jones, L., Reynolds, J., Hornsby, P., & Powell J.(2013). Control trial and fecal egg count reduction test determinations of nematocidal efficacies of moxidectin and generic ivermectin in recently weaned, naturally infected calves. *Vet. Parasitol.* , 195, 95-101.
- Yazwinski, T.A., Williams, J.C., Smith, L.L., Tucker, C., Loyacano, A.F., DeRosa, A., Peterson, P., Bruer, D.J., & Delay, R.L. (2006). Dose determination of the persistent activity of moxidectin long- acting injectable formulations against various nematode species in cattle .*Vet. Parasitol.*, 137, 273-285.

## **CHAPTER 1**

### **Evaluation of anthelmintic therapies in a fall calving beef cowherd**

#### **INTRODUCTION**

It has been reported that conservatively, the economic losses in the cattle industry due to gastro-intestinal nematode parasitism reaches upwards of \$2 billion per year in terms of productivity losses and increased production expenses, not including the costs associated with increased labor due to increased animal handling (Stomberg and Gasbarre, 2006). Unfortunately, it is understood that the actual losses are much greater as this estimation can only factor in observed, quantifiable losses and does not account for other subclinical losses which are believed to be even greater than what is actually measurable (Myers, 1988). There are three different forms of internal parasitism that can affect our cattle which are defined as: infection, economic, and clinical forms. In this ideology, production losses that are due to the internal parasitic infections in cattle, which are not apparent to the producers, falls into the economic form. These are believed to greatly exceed those losses that are obvious by mortality or the state of disease, which would be considered the clinical form of parasitism. Out of the three forms of parasitism, the economic form is believed to be by far the most challenging to assess due to the fact that the animal physically looks healthy, but without comparing performance of treated animals to control animals, the true impact would still be greatly unknown (Craig, 1988). This underestimation of economic production losses coupled with increasing resistance to many anthelmintic products poses a major threat to the ability to maintain the health and productivity of cattle against parasitic infections. Of the many species of parasites that are a concern for cattle productivity, those that warrant the most attention are known as the Trichostrongyles.

Various species within the subfamily Trichostrongylidae have been observed to show resistance to anthelmintic products of all drug classes due to continuous administration, which perpetuates selection driven resistance at an accelerated rate. With this knowledge, there has been much investigation into the commercially available extended release formulation of eprinomectin, which has a label indicating up to 150 days of efficacy against nematode infections in cattle after only one injection. This extended activity appears very beneficial for both the animal and the producer where the animal receives extended protection from parasite infections due to a “broken” infection process, and the producer saves money in labor costs from decreased gathering of cattle for treatment. Another advantage of an extended activity anthelmintic product is the possibility to slow down the rate of resistant nematode generation turnover with longer periods occurring between treatments compared to other commercially available products. (Rehbein et al., 2013).

Therefore, the purpose of this study was to evaluate performance and fecal nematode egg reduction for cows and calves when administered either extended release eprinomectin or moxidectin anthelmintic therapies just prior to calving; as well as to evaluate performance and fecal nematode egg reduction for calves administered fenbendazole 55 days prior to weaning.

## **MATERIALS AND METHODS**

### **Location and Animals**

This study was conducted at the University of Arkansas Cow Calf unit in Savoy, Arkansas and consisted of 106 multiparous beef cows and their respective calves. All cows used in this study were of an Angus cross breed type. Authorized farm personnel monitored animals on a daily basis throughout the time of the study. Prior to the beginning of the study, all methods

and procedures were approved by the University of Arkansas' Institutional Animal Care and Use Committee (approval # 19014).

## **Experimental Design**

### *Cow Management*

This study consisted of a randomized block design in which 106 resident fall calving multiparous beef cows were stratified by weight and parity, before being randomly allocated to 3 different treatment groups: negative control (CON), injectable moxidectin (MOX), and injectable extended release eprinomectin (ERE). Sample size of cow treatment groups are as follows: CON (n =38), MOX (n = 30), and ERE (n =38). Cows in the CON group served as negative control and did not receive any treatment. Cows in the MOX and ERE treatments groups were administered their respective anthelmintics following label instructions on dose measurements and route of administration. Cows in the MOX treated group received subcutaneous injections of 1% sterile moxidectin (Cydectin®, Bayer HealthCare LLC, Shawnee Mission, KS) at a dose of 0.2 mg/kg of bodyweight in the cranial portion of the shoulder. Cows in the ERE treated groups received subcutaneous injections of 5% sterile eprinomectin (LongRange®, Merial Limited, Duluth, GA) at a dose of 1.0mg/kg of bodyweight in the cranial portion of the shoulder as well. Treatment was administered one week prior to fall calving in September 2018. Cows were left to comeingle while grazing on permanent pastures throughout the duration of the study, unless being brought in for days where sampling occurred and with the exception of subgroup pasturing during the breeding periods. Pastures were primarily comprised of a mixture between warm season Bermudagrass and cool season endophyte – infected tall Fescue. Unequal cow numbers in the MOX treatment group compared to the ERE treatment and CON group resulted due to animal allocation to the study prior to gaining knowledge that some cows within the herd who

had been previously confirmed pregnant were veritably open, as well as some naturally occurring calf loss after birth. These animals who were open or who lost calves were removed from the previously allocated group and therefore were not included in the study.

On d0, cows were brought in from the pastures and processed through a chute to identify the animal according to its ear tag to confirm treatment group placement. Cows were then treated with their respective anthelmintic, a fecal sample was obtained, bodyweights (BW) and body condition scores (BCS) were recorded. All cows were worked through the chute in this fashion on d 80, d 162, and d 217 of the study with weaning occurring on d 217. All fecal samples were stored at 4°C prior to being processed for FEC determination, expressed as eggs per gram (EPG).

#### *Calf Allocation*

Farm personnel processed 106 Angus crossbred fall born calves from the group of cows (n = 106) previously included in the study, as mentioned above. The fall calving season occurred from September 2018 to November 2018, in which time all calves were processed with a unique identification tag and had their birth weights recorded. Once processing was completed calves within each dam treatment group were stratified by weight and sex before being randomly allocated to a group of either negative control (CON) or oral fenbendazole drench (FEN) for later treatment. Of the 106 fall calves 46 of the calves were female and 60 of the calves were male. The 38 calves born from the CON group was comprised of 17 female calves and 21 male calves. The 30 calves born from the MOX group was comprised of 11 female calves and 19 male calves. The 38 calves born from the ERE group was comprised of 18 female calves and 20 male calves. Of the 106 processed calves 53 were allocated to the CON group and 53 were allocated to the FEN group. The CON group was comprised of 22 female calves and 31 male calves while the FEN group was comprised of 24 female calves and 29 male calves.

### *Calf Management*

From d 0 to d 80 calves that were born were processed as mentioned above. On d 80 calves were brought in from the pastures and were individually processed through a chute to identify the animal according to its ear tag to confirm treatment group placement. Calves, ranging from 1 month to 3 months of age, had their body weights recorded and received respiratory vaccinations (Pyramid 5, Boehringer Ingelheim, Vetmedica, Inc., St. Joseph, MO). On d 162 of the study, calves ranging from 4 to 6 months of age were worked individually through a chute to record body weights, obtain fecal samples and be administered anthelmintic treatment according to their assigned group. Calves that were allocated to controls were not treated and those that were allocated to FEN group were orally drenched with Fenbendazole (Safeguard®, Intervet Inc., Madison, NJ) at 5 mg/kg of body weight. At the time of weaning, d 217 of the study, calves were again processed through a chute to administer a second round of respiratory vaccinations, record body weights and obtain fecal samples for fecal egg count quantification. Calf ages ranged from 6 to 8 months of age at the time of weaning. All fecal samples were stored at 4°C prior to being processed for FEC determination, expressed as eggs per gram (EPG).

### *Fecal Egg Count*

Fecal samples were obtained directly from the rectum, by a poly shoulder length glove and then compressed to release excess air before sealing. These samples were taken directly to the University of Arkansas Parasitology lab to be analyzed for a FEC using 1 gram of feces and a magnesium sulfate (MgSO<sub>4</sub>) direct centrifugation- floatation technique. This technique was performed for all cows and calves with cow fecal samples occurring on d 0, 80, 162, 217 and calf fecal samples occurring on d 162 and 217. One gram of fecal material from each animal was broken up with metal spatula. Fifteen mL of magnesium sulfate (MgSO<sub>4</sub>) was added to the feces

solution and hand homogenized with a metal spatula before straining through a 1 mm aperture sieve to remove large debris particles. The fecal solution was then placed in 15 mL test tubes and topped with a coverslip (22× 22 mm) before centrifugation for egg floatation. The coverslip was then removed and placed on a microscope slide to be viewed for egg quantification using a microscope at 40x magnification. Eggs were counted and recorded on a per gram basis (EPG).

### *Statistical Analysis*

Quantitative measures for cow data included: BW, BCS, FEC, calving date and calving rate. Quantitative measures for calf data included: birth weight, BW, ADG, FEC, 205 day adjusted weaning weight, and gender frequency by treatment. These quantitative measures were analyzed using a mixed procedure of SAS. Fecal egg count values were transformed into log FEC values and transformed back to geometric means (GM) by taking the inverse of ( $\log_{10}(x) - 1$ ) for construction of the upcoming tables and figures. A 205 day adjusted weaning weight was calculated to adjust calf wean weights in order to allow for a fair age equivalent comparison among calves weaned between the ages of 160 – 250 days of age (Gould , 2015). This was calculated by using the following equation: (calf WW – calf birth weight)/ (wean date – calving date) \* 205 + calf birth weight. Contrast statements were made for CON vs. Treated and MOX vs. ERE groups.

Qualitative data such as pregnancy rate and calf gender frequency rate by treatment, was analyzed using GENMOD with a binomial distribution. Fixed effects for cow data was dam treatment, day, and day × treatment. The experimental unit was the cow. For calf data fixed effects were calf treatment, day, dam treatment, calf × dam treatment, and calf treatment × dam treatment × day. The experimental unit was the calf. All differences were considered with a  $P \leq 0.05$  significance and tendencies were considered at  $0.05 \leq P \leq 0.10$ .

## RESULTS

### Cow Performance Results

#### *Body Weights (BW)*

In this study, weight gain was recorded to determine if treatment with ERE pre calving would result in greater weight gain than cows treated with MOX. Cow body weights followed a similar trend of day effect ( $P < 0.0001$ ) from d 0 to d 217 from the time of calving to weaning with an average bodyweight of ( $544.1 \pm 4.5$  kg) and did not differ ( $P = 0.97$ ) in regards to a dam treatment by day interaction. An orthogonal contrast statement revealed no difference of control versus treatment effect on cow BW ( $P = 0.38$ ). There was also no observed effect of MOX treatment versus ERE treatment on cow BW ( $P > 0.92$ ) ( Table 1; Figure 1). Pooled average body weight of cows from all treatments on d 0 was ( $573.8 \pm 8.7$  kg) and did not differ ( $P = 0.97$ ). From d 0 to d 80 all cows across treatments lost weight with a pooled average of ( $530.4 \pm 10.8$  kg) and did not differ ( $P = 0.57$ ). From d 80 to d 162 cows across all groups showed similar gain with a pooled average of ( $555.2 \pm 8.2$  kg) and did not differ ( $P = 0.89$ ). From d 162 to d 217, a similar loss in weight was observed across all treatments with a pooled average of ( $517.2 \pm 7.8$  kg) and did not differ ( $P = 0.90$ ). ( Table 1; Figure 1).

#### *Body Condition Scores (BCS)*

Cow BCS also followed a similar trend of day effect ( $P < 0.0001$ ) from d 0 to d 217 from the time of calving to weaning; with an average BCS of ( $5.4 \pm 0.5$ ), and with no observed difference on cow treatment by day interaction ( $P = 0.92$ ). There was, however, an observed tendency ( $P = 0.08$ ) for dam treatment to have an effect on BCS. An orthogonal contrast statement of control versus treated revealed observed differences ( $P = 0.03$ ) on cow BCS, where CON cattle were found to have lower BCS than those treated cattle. An orthogonal contrast



statement of MOX versus ERE cattle treatment had no observed differences ( $P = 0.48$ ) on cow BCS. (Table 2; Figure 2). On d 0 pooled average BCS across all treatments was ( $6.8 \pm 0.1$ ) and did not differ ( $P = 0.23$ ). From d 0 to d 80 cows across all treatments experienced a similar loss of condition with a pooled average BCS of ( $5.4 \pm 0.1$ ) and did not differ ( $P = 0.82$ ). From d 80 to d 162 cows across all treatments again experienced a similar loss of condition with a pooled average BCS of ( $5.0 \pm .1$ ) and did not differ ( $P = 0.22$ ). Lastly, from d 162 to d 217 cows across all treatments experienced an even greater loss of condition with a pooled average BCS of ( $4.3 \pm 0.2$ ) and did not differ ( $P = 0.48$ ). (Table 2; Figure 2).

#### *Cow fecal egg counts*

The observed geometric means of cow fecal egg counts were overall lower for ERE treated cattle ( $P = 0.003$ ) from d 0 to d 217 of the study where the average FEC for ERE treated cattle was ( $1.3 \pm 0.1$  epg) ; ( $2.1 \pm 0.1$  epg) for MOX treated cattle and ( $2.3 \pm 0.1$  epg) for CON cattle. An orthogonal contrast statement of control versus treated revealed observed differences ( $P = 0.03$ ) on cow FEC, where CON cattle were found to have higher FEC than those treated cattle. An orthogonal contrast statement of MOX versus ERE cattle treatment also observed differences ( $P = 0.007$ ) on cow FEC, where ERE treated cattle had lower FEC compared to MOX treated cattle (Table 3). On d 0 pooled average of FEC across all treatments was ( $2.4 \pm 0.2$  epg) and did not differ ( $P > .35$ ). On d 80 control cows had a higher FEC observed than that of extended release eprinomectin and moxidectin treated cattle ( $P < 0.0001$ ), but FEC of MOX treated cattle did not differ from ERE treated cattle ( $P = 0.16$ ). FEC of treatments are as follows for ERE, MOX, and CON cows:  $1.0 \pm 0.1$  epg;  $1.9 \pm 0.1$  epg; and  $5.0 \pm 0.1$  epg. On d 162 pooled average FEC across all treatments was ( $1.6 \pm 0.2$  epg) and did not differ ( $P = 0.40$ ). On d 217

pooled average FEC across all treatments was ( $0.9 \pm 0.2$  epg) and did not differ ( $P = 0.45$ ) (Table 3).

#### *Cow reproductive performance*

Cow reproductive performance was measured by data acquired from both fall 2018 and subsequent 2019 fall calving seasons. Fall 2018 reproductive performance was measured by calf birth date and gender frequency distribution, while subsequent fall 2019 reproductive performance was measured by percent pregnant by natural breeding, percent pregnant by artificial insemination, overall pregnancy rate, subsequent fall calving rate and subsequent fall 2019 calving date. There was no observed difference on fall 2018 calf birth date by dam treatment ( $P = 0.96$ ). There were also no observed differences on control versus treated ( $P = 0.96$ ) or MOX versus ERE ( $P = 0.79$ ) dam treatment effect on fall 2018 calf birth date (Table 4). Total herd calf crop which was comprised of calves from CON, MOX and ERE dam treatment groups yielded 106 calves, which was composed of 43% female calves and 57% male calves. Of the 38 calves born from the CON dam group, 45% were females and 55% were males. Of the 30 calves born from the MOX dam group, 37 % were females and 63 % were males. Of the 38 calves born from the ERE dam group, 47% were females and 53% were males.

Overall pregnancy rate for the fall 2019 calving season was 84% with pregnancy rates per treatment group ERE, MOX, and CON cows as follows: 92, 77, and 82 %. There was no observed anthelmintic effect on pregnancy rates across all treatments ( $P = 0.17$ ) or effect on control vs. treated groups ( $P = 0.55$ ); however, there was an observed tendency ( $P = 0.07$ ) for ERE treated cows to have higher pregnancy rates than that of MOX treated cows (Table 5). Overall calving rate for the fall calving cow herd was 81% with calving rates per treatment group ERE, MOX, and CON cows as follows: 92, 67, and 82%. There was an observed difference in

calving rate amongst the three treatments ( $P = 0.02$ ) where ERE treated cattle had higher calving rates than those that were treated with MOX ( $P = 0.007$ ). However, there was no observed difference in calving rates between control and treated groups ( $P = 0.87$ ). (Table 5; Figure 3). There was no observed anthelmintic effect on percent pregnancies confirmed by natural breeding among treatments ( $P = 0.29$ ), or by artificial insemination pregnancies ( $P = 0.17$ ); however, there was an observed tendency ( $P = 0.06$ ) for CON cows to have fewer AI confirmed pregnancies than treated cows. (Figure 4). There was no observed difference in anthelmintic effect on the following seasons' calving date ( $P = 0.23$ ), but there was an observed trend for treated cows to calve earlier than cows that were left as negative controls ( $P = 0.11$ ) (Table 6).

## **Calf performance results**

### *Birth weights*

Calf birth weights were similar and did not differ among dam treatments: CON, MOX, or ERE ( $P = 0.14$ ). Mean calf birth weights from CON, MOX, and ERE groups were:  $32.0 \pm 0.8$  kg;  $32.5 \pm 0.9$  kg;  $34.2 \pm 0.8$  kg, respectively (Figure 5).

### *Body Weights (BW)*

Calf weights were similar among FEN and CON treatments for d 162 ( $P = 0.53$ ) and were not affected by a dam treatment of either CON, MOX, or ERE ( $P = 0.75$ ). A similar trend was observed for body weights of FEN and CON calf treatments on d 217 ( $P = 0.81$ ) and were again not affected by a dam treatment ( $P = 0.91$ ). On d 162 CON calves weighed an average of ( $179.1 \pm 5.4$  kg) while FEN treated calves weighed an average of ( $182.3 \pm 5.3$  kg). On d 217 CON calves weighed an average of ( $221.2 \pm 10.3$  kg) while FEN treated calves weighed an average of ( $222.6 \pm 10.3$  kg) (Figure 6).

#### *Average Daily Gain (ADG)*

Calf ADG was observed to be similar between FEN and CON treatments from d 162 to d 217 ( $P = 0.47$ ) and was not affected by a dam treatment ( $P = 0.36$ ). Control calves gained an average of ( $0.76 \pm 0.1$  kg/ day) while FEN treated calves gained an average of ( $0.73 \pm 0.1$  kg/ day) (Figure 7).

#### *Calf 205-day adjusted weaning weight*

Observed calf 205-day adjusted weaning weights were similar and did not differ among FEN and CON calves in relation to dam treatment ( $P = 0.14$ ), calf treatment ( $P = 0.92$ ), and calf treatment  $\times$  dam treatment interaction ( $P = 0.70$ ). Mean calf 205 day adjusted weaning weight was ( $206.5 \pm 3.5$  kg) for the CON group and ( $207.0 \pm 3.5$  kg) for the FEN treated group. An orthogonal contrast statement for CON versus Treated dams, both MOX and ERE combined, did reveal a strong tendency ( $P = 0.0516$ ) for dam treatment to have an effect on calf 205-day adjusted weaning weights (Figure 8). However, an orthogonal contrast statement of MOX versus ERE observed no differences ( $P = 0.93$ ) on 205-day adjusted weaning weight of calves. Mean 205-day adjusted weaning weights of calves according to CON,MOX, and ERE dam treatment groups were:  $200.0 \pm 4.1$  kg;  $209.9 \pm 4.7$  kg;  $210.4 \pm 4.1$  kg, respectively (Figure 9).

#### *Calf fecal egg counts*

Observed calf fecal egg counts were similar ( $P = 0.19$ ) among FEN and CON treatments on d 162, where CON calves had an average ( $9.8 \pm 0.1$  epg) while FEN treated calves had an average ( $12.0 \pm 0.1$  epg). On d 217, calves in FEN treated and control groups had a similar FEC ( $P = 0.79$ ) where CON calves had an average ( $17.8 \pm 0.4$  epg) while FEN treated calves had an average ( $17.1 \pm 0.4$  epg) (Figure 10).

Though FEC were similar among FEN and CON calves in relation to calf treatment on d 162; there was however, an observed tendency for calf FEC to differ in relation to dam treatment ( $P = 0.08$ ). On d 162 calves born from ERE treated dams had a lower FEC than calves born from CON dams ( $P = 0.03$ ) where calves from ERE dams had an average ( $9.3 \pm 0.1$  epg) and calves from control dams had an average ( $13.5 \pm 0.1$  epg). Calves born from MOX treated dams had an intermediate FEC of ( $10.1 \pm 0.1$  epg) that did not differ significantly from the FEC of the calves from the CON ( $P = 0.14$ ) or ERE ( $P = 0.7$ ) dam groups (Figure 11).

## **DISCUSSION**

Observations of increasing anthelmintic resistance in parasites have driven the exploration for long-term solutions for nematode control in livestock species. In this study, there were two objectives: 1.) To evaluate the efficacy of two classes of commercially available macrocyclic lactones on beef cattle performance over a period of 217 days; 2.) To evaluate the egg count and performance effects of fenbendazole treated and non- treated control calves 55 days before weaning.

### **Cow Performance Discussion**

In this study, weight gain and body condition scores were evaluated to determine if treatment with ERE would result in a greater weight gain as compared to animals treated with MOX or those left as controls. The collection of body weight and condition score changes over a given time period are important aspects in determining cattle's nutritional status (Ndlovu et al., 2007) as well as overall health (Berry et al., 2006) and fertility (Buckley et al., 2003). The observational trend in similar loss of body weight and body condition score across all cow treatments in relation to a day effect from d 0 to d 80 is most likely attributed to the period of calving and peak lactation that occurred during this time frame. Observed similarities in body

weight and body condition scores across cow treatments throughout the study is most likely attributed to the low worm burdens reflected by the low fecal egg counts observed in cows across all groups, indicating only a minor impact of worm infections on animal performance.

Though we did not see sizeable effects of anthelmintic treatment on cow body weights or body condition scores throughout the duration of the study we did see an effect on cow fecal egg counts. Although fecal egg counts were considered extremely light throughout the duration of the study, ERE treated cows had overall lower fecal egg counts compared to MOX and CON cows throughout the study. On d 80 there was observed differences between CON and anthelminthic treated cows, where ERE and MOX treated cows had lower FEC than CON cows. Though the FEC for MOX treated cows was greater than that of ERE treated cows, there were no observed differences between these two groups. For CON cows these results are most likely attributed to the further natural pasture infection that would increase in an animal without the use of an anthelmintic treatment. For MOX treated cows these results would be attributed to the decrease in internal nematode populations upon initial treatment that would have provided an estimated 14 to 42 days of internal nematode protection as stated in product label claims. This would have allowed for a reinfection period to occur, prior to secondary fecal collection on d 80. For ERE treated cows these results would be attributed to the decrease in internal parasitism populations upon initial treatment that would have provided anywhere from 100-150 days of internal nematode protection as stated in the product label claims.

As stated in earlier results, dam treatment in fall 2018 prior to calving did not have an observed effect on fall 2018 calving dates. This is likely attributed to the late phase of gestation that dams had already reached at the time of treatment administration. It was also stated earlier

that calf gender frequency distribution among treatments was unaffected by dam treatment in the fall 2018 calf crop.

Though there were no observed effects of fall 2018 cow treatment on cow reproductive performance for the fall 2018 calving season, there was observed differences for the subsequent, fall 2019, calving season. In this study, it was observed that those previously ERE treated cows with lower FEC had an observed tendency for higher pregnancy rates in the 2019 fall calving season compared to those previously MOX treated cows. In addition to this, there was also an observed effect on calving rate, where cows treated with ERE in the previous fall had a higher fall 2019 calving rate than those treated with MOX. This may indicate that the effect on worm burdens had a possible effect on dam immunity. If a cow's immunologic and resilience homeostatic mechanisms are not being taxed by worm infection, such as in the ERE cattle, then the cycling cow would have an increased ability to conceive, as disturbed immune function has been identified as a primary component to infertility (Fair, 2015).

Future studies should focus on the investigation of interactions between fecal egg counts and immune status within cycling beef cows. The observed tendency which reflects a higher pregnancy rate and calving rate in ERE treated cows compared to MOX treated cows could be partly attributed to the fact the sample size of MOX cows in this study was smaller than the CON and ERE groups. Though there was an observed tendency for higher fall 2019 pregnancy rates in relation to cow treatment, little effects were observed in relation to proportion of pregnancy percentage by natural and artificial insemination of cows within treatment groups. Although there was an observed tendency for CON cows to have fewer A.I. confirmed pregnancies compared to MOX and ERE groups, upon further investigation into Figure 4, one can see that the proportion of naturally acquired pregnancies within this group was larger than that of MOX and

ERE treated groups. Lastly, for cow reproductive performance, it is important to note the observed trend in calving date differences among cow treatment groups. In this study, there was an observed trend for CON cows to calve later in the subsequent 2019 calving season compared to those cows that were treated previously in 2018. Note, that earlier it was stated that in this study, there was an observation that CON cows also tended to have a lower BCS throughout the project duration. This may indicate that in this study there was an observed interaction between a lower BCS and a later subsequent calving date. This interaction is supported by previous literature (Herd and Sprott, 1986) that states a lower BCS post calving prompts an extended period before a return to estrus, thus extending both the time until a future confirmed pregnancy and subsequently, the calving interval.

### **Calf Performance Discussion**

In this study, there was no observed difference in FEN treated or CON calves in regards to body weight or average daily gain over the 55 days prior to weaning. These production parameters were also unaffected by previous dam treatment, which could be due to the fact that both dams and calves, in all treatment groups, had low level parasitic infections throughout the study period.

In this study, there was also no observed effect on calf birth weight, which is again most likely attributed to the short interval between dam treatment and calf birth. There was however, observed differences on calf 205-day adjusted calf weaning weight and calf FEC in relation to dam treatments. In the results, it is observed that the calves born from anthelmintic treated cows had an additional 9.95 kg of body weight in their 205-day adjusted weaning weight compared to calves born from CON cows who did not receive any treatment. In addition to this, it was also observed that calves born from ERE treated cattle had a tendency for lower FEC at d 162 of the



study compared to calves that were born from CON cows. The implications here are that pre-calving anthelmintic treatment of the dam could be beneficial in order to increase weaning weight and curtail calf worm burden in a beef cow calf operation. Both a higher weaning weight and lower worm burden could lend a hand in a greater immune competence of the calves, which may enhance their ability to gain weight and fight parasitic infections after the weaning period. Future studies should investigate if prior dam anthelmintic treatment will go on to affect calf performance measurements and FEC from the time of birth until the end of the stocker /beginning of the feedlot phase.

## **CONCLUSION**

In conclusion, though there were not many observed treatment associated differences in this study, there is still need for further investigations of anthelmintic intervention and resultant performance of cow calf pairs who are naturally infected with internal parasites. These studies should include animals with higher, and more common levels of parasitic infection to accomplish a moderate infection (200 to 800 eggs per gram), in order to get an accurate observation of parasitic effect on performance prior to treatment. With infection levels similar to these very light infections observed in this study, it would not be in the producer's best interest to treat cows with an anthelmintic. Treatment of animals with anthelmintic products at low infection levels significantly increases the likelihood of producing genetically resistant worms, while at the same time not reaping the benefits of curbing economically significant levels of parasitism. However, a producer should still strive to maintain parasitism below economic thresholds, a scenario that requires regular treatments.

In the same way that no two cow calf operations are the same, parasitic infections in livestock between operations can differ greatly as well. Producers must make their own decisions

to combat internal parasitism within their herd based on their resources, time, and acceptable associated costs. With the ever increasing prevalence of anthelmintic resistance in our livestock (Kaplan and Vidyashankar, 2012), it is becoming increasingly more important to strategically combat internal parasitism by using multifaceted integrated parasite management systems (Maqbool et al., 2017). Now more than ever the agricultural community can prosper from current and future studies like this one, which investigates the efficacy of the anthelmintic products available to ensure animal performance measures are continuing to be met in order to feed our increasing population both in the U.S. and around the world.

## REFERENCES

- Berry D.P., Macdonald, K.A., Penno, J.W., & Roche, J.R. (2006). Association between body condition score and live weight in pasture-based Holstein-Friesian dairy cows. *J. Dairy Res.*, 73, 487-491.
- Buckley F., O'Sullivan, K., Mee, J.F., Evans, R.D., & Dillon, P. (2003). Relationships among milk yield, body condition, cow weight, and reproduction in spring-calving Holstein-Friesians. *J. Dairy Sci.*, 86, 2308-2319.
- Craig, T.M. (1988). Impact of internal parasites on beef cattle. *J. Anim. Sci.*, 66., 1565-1569.
- Fair, T.(2015). The contribution of the maternal immune system to the establishment of pregnancy in cattle. *Front. Immunol.*, 6, 1- 8.
- Gould, K. (2015, August). Calculating calf- adjusted weaning weights and herd indexes. *MSU Extension*. Retrieved from [https://www.canr.msu.edu/news/calculating\\_calf\\_adjusted\\_weaning\\_weights\\_and\\_herd\\_indexes](https://www.canr.msu.edu/news/calculating_calf_adjusted_weaning_weights_and_herd_indexes)
- Herd, D.B., & Sprott, L.R. (1986). Body condition, nutrition, and reproduction of beef cows. Texas Agricultural Extension Service (B- 1526). Texas A & M University Library. 3-11.
- Kaplan, R. M., & Vidyashankar, A.N. (2012). An inconvenient truth: Global warming and anthelminic resistance. *Vet. Parasitol.*, 186, 70-78.
- Maqbool, I., Wani, Z.A., Shahardar, R.A., Allaie, I.M., & Shah, M.M. (2017). Integrated parasite management with special reference to gastro-intestinal nematodes. *J. Parasit. Dis.*, 41, 1-8.
- Myers, G.H. (1988). Strategies to control internal parasites in cattle and swine. *J. Anim. Sci.*, 66, 1555-1564

- Ndlovu T., Chimonyo, M., Okoh, A. I., Muchenje, V., Dzama, K., & Raats, J.G.(2007). Assessing the nutritional status of beef cattle: current practices and future prospects. *Afr. J. Biotechnol.*, 6, 2727-2734.
- Rehbein, S., Baggott, D.G., Johnson, E.G., Kunkle, B.N., Yazwinski, T.A., Yoon, S., Cramer, L.G., & Soll, M.D. (2013). Nematode burdens of pastured cattle treated once at turnout with eprinomectin extended-release injection. *Vet. Parasitol.*, 192, 321-331.
- Stromberg, B. E., & Gasbarre, L.C. (2006). Gastrointestinal Nematode Control Programs with an Emphasis on Cattle. *Vet Clin Food Anim* , 22, 543-565.
- Wagner, J.J., Lusby, K.S., Oltjen, J.W., Rakenstraw, J., Wettemann, R.P., & Walters, L.E. (1998). Carcass composition in mature Hereford cows: estimation and effect on daily metabolizable energy requirement during winter. *J. Anim. Sci.*, 66, 603 -612.

Table 1. Bodyweight (BW) measurements of fall calving multiparous beef cows treated prior to calving with either Moxidectin or Extended Release Eprinomectin

Item	Treatments <sup>a</sup>			SEM <sup>b</sup>	<i>P</i> -Value <sup>c</sup>	CON VS TREATED <sup>d</sup>	MOX VS ERE <sup>d</sup>
	MOX	ERE	CON				
BW, kg							
d0	575.4	573.7	572.1	8.7	0.97	0.85	0.90
d80	530.4	539.7	521.3	10.8	0.57	0.99	0.29
d162	559.1	553.7	552.7	8.2	0.89	0.64	0.94
d217	520.7	515.6	515.4	7.8	0.90	0.66	0.98
Overall	546.4	545.7	540.4	4.5	0.97	0.38	0.92

<sup>a</sup> CON= control; MOX= moxidectin; ERE= extended release eprinomectin

<sup>b</sup> SEM= pooled SEM

<sup>c</sup> Cow BW, total gain, BCS, and FEC were analyzed using MIXED procedures of SAS

<sup>d</sup> CON VS TREATED and MOX VS ERE values were analyzed by orthogonal contrasts

\*No significant differences were noted

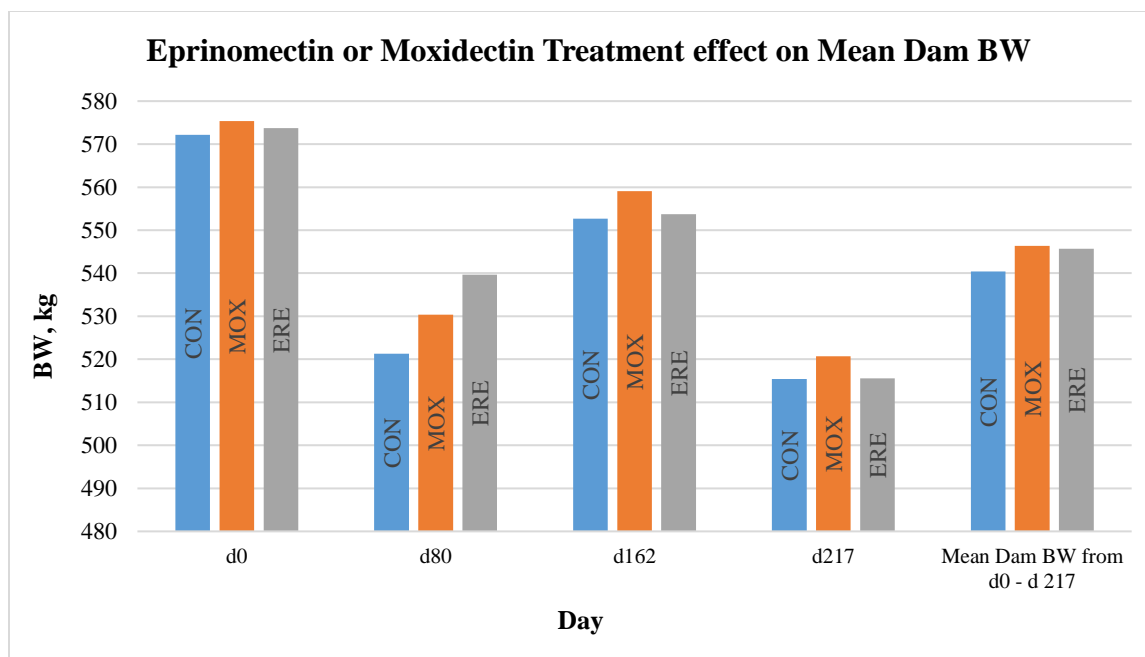


Figure 1. Mean ( $\pm$ SEM) weights (kg) of cow treatment groups: control, injectable moxidectin (0.2mg/kg of BW); injectable extended release eprinomectin (1mg/kg of BW) recorded on d0, 80, 162, and 217 of the study. N=38 CON; 30 MOX; 38 ERE cows per treatment group.

\*No significant differences were noted

Table 2. Body Condition Score (BCS) measurements of fall calving multiparous beef cows treated prior to calving with either Moxidectin or Extended Release Eprinomectin

Item	Treatments <sup>a</sup>			SEM <sup>b</sup>	P-Value <sup>c</sup>	CON VS TREATED	MOX VS ERE
	MOX	ERE	CON				
BCS <sup>d</sup>							
d0	6.9	6.8	6.6	0.1	0.23	0.21	0.23
d80	5.4	5.4	5.3	0.1	0.82	0.74	0.59
d162	5.1	4.9	4.9	0.1	0.22	0.08	0.83
d217	4.4	4.4	4.1	0.2	0.48	0.67	0.25
Overall	5.4 <sup>x</sup>	5.4 <sup>x</sup>	5.2 <sup>y</sup>	0.1	0.08	0.03	0.48

<sup>a</sup> CON= control; MOX= moxidectin; ERE= extended release eprinomectin

<sup>b</sup> SEM= pooled SEM

<sup>c</sup> COW BW, total gain, BCS, and FEC were analyzed using MIXED procedures of SAS

<sup>d</sup> 1 to 9 scale; 1= emaciated; 9= obese; (<sup>14</sup>Wagner et al., 1998)

<sup>x,y</sup> Means within a row without common superscripts tended to differ ( $0.05 < P < 1.0$ )

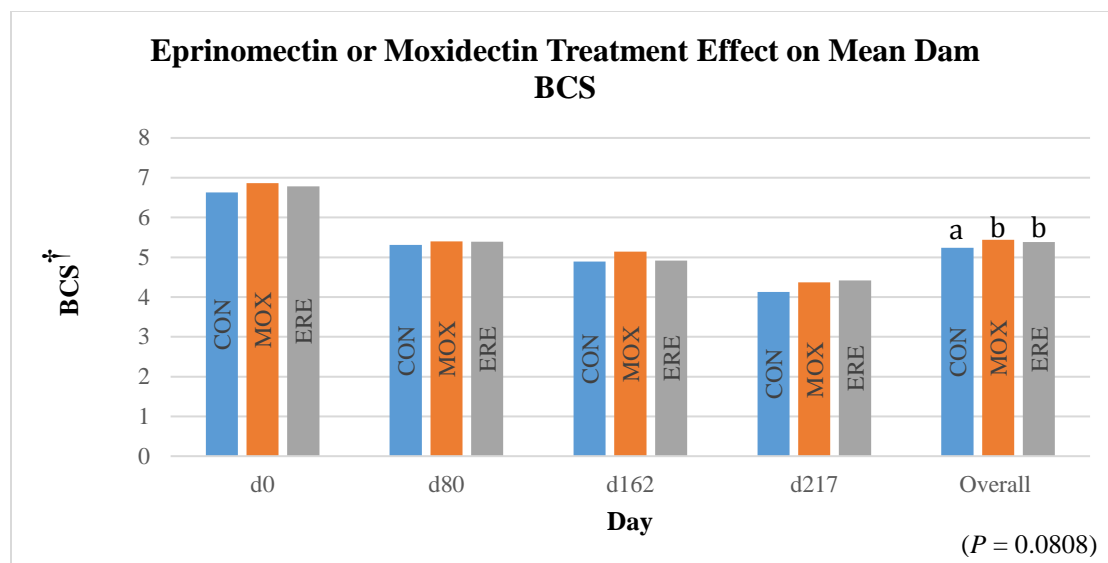


Figure 2. Mean ( $\pm$ SEM) BCS of cow treatment groups: control; injectable moxidectin (0.2mg/kg of BW); injectable extended release eprinomectin (1mg/kg of BW) recorded on d0, 80, 162, and 217 of the study. N=38 CON; 30 MOX; 38 ERE cows per treatment group.

†BCS measured using 1 to 9 scale; 1= emaciated; 9= obese; (Wagner et al., 1998)

<sup>a,b</sup>Means without common superscripts tended to differ ( $0.05 < P < 0.10$ )

Table 3. Fecal egg count (geometric means; GM) treatment  $\times$  day interaction of fall calving multiparous beef cows treated prior to calving with either Moxidectin or Extended Release Eprinomectin

Item	Treatments <sup>a</sup>			SEM <sup>b</sup>	<i>P</i> -Value	CON VS TREATED	MOX VS ERE
	MOX	ERE	CON				
Overall FEC, GM <sup>c</sup>	2.1 <sup>d</sup>	1.3 <sup>e</sup>	2.3 <sup>df</sup>	0.1	0.0031	0.03	0.007
d0 (calving)	3.1 <sup>g</sup>	2.0 <sup>g</sup>	2.2 <sup>g</sup>	0.2	0.35	0.64	0.16
d80	1.9 <sup>hi</sup>	1.0 <sup>ih</sup>	5.1 <sup>j</sup>	0.2	<0.0001	<0.0001	0.16
d162	2.0 <sup>k</sup>	1.3 <sup>k</sup>	1.6 <sup>k</sup>	0.2	0.40	0.88	0.18
d217 (weaning)	1.5 <sup>l</sup>	0.9 <sup>l</sup>	1.3 <sup>l</sup>	0.2	0.45	0.89	0.22

<sup>a</sup>CON= control; MOX= moxidectin; ERE= extended release eprinomectin

<sup>b</sup>SEM= pooled SEM

<sup>c</sup>FEC= fecal egg counts

<sup>d-l</sup>Means within a row without common superscripts differ ( $P < 0.05$ )



Table 4. Fall 2018 average calving date  $\times$  dam treatment interaction of multiparous beef cows treated prior to calving in fall 2018 with either Moxidectin or Extended Release Eprinomectin

Item	Treatments <sup>a</sup>		CON	<i>P</i> -Value	CON VS TREATED	MOX VS ERE
	MOX	ERE				
Calving Date	9/25/18	9/26/18	9/26/18	0.96	0.96	0.79

<sup>a</sup>CON= control; MOX= moxidectin; ERE= extended release eprinomectin

\*No significant differences were noted

Table 5. Subsequent (fall 2019) reproductive performance measurements of multiparous beef cows treated prior to calving in fall 2018 with either Moxidectin or Extended Release Eprinomectin

Item	MOX	Treatments <sup>a</sup>		SEM <sup>b</sup>	<i>P</i> -Value <sup>c</sup>	CON VS TREATED	MOX VS ERE
		ERE	CON				
Pregnancy Rate <sup>d</sup> , %	77	92	82	---	0.18	0.55	0.07
Calving Rate <sup>e</sup> , %	67 <sup>xz</sup>	92 <sup>y</sup>	82 <sup>zy</sup>	---	0.03	0.87	0.007

<sup>a</sup> CON= control; MOX= moxidectin; ERE= extended release eprinomectin

<sup>b</sup> SEM= pooled SEM

<sup>c</sup> Pregnancy rate and calving rate was analyzed using GENMOD

<sup>d</sup> Percent cows confirmed pregnant within each treatment

<sup>e</sup> Percent cows that calved within each treatment group

<sup>x-z</sup> Means within a row without common superscripts differ ( *P* < 0.05)

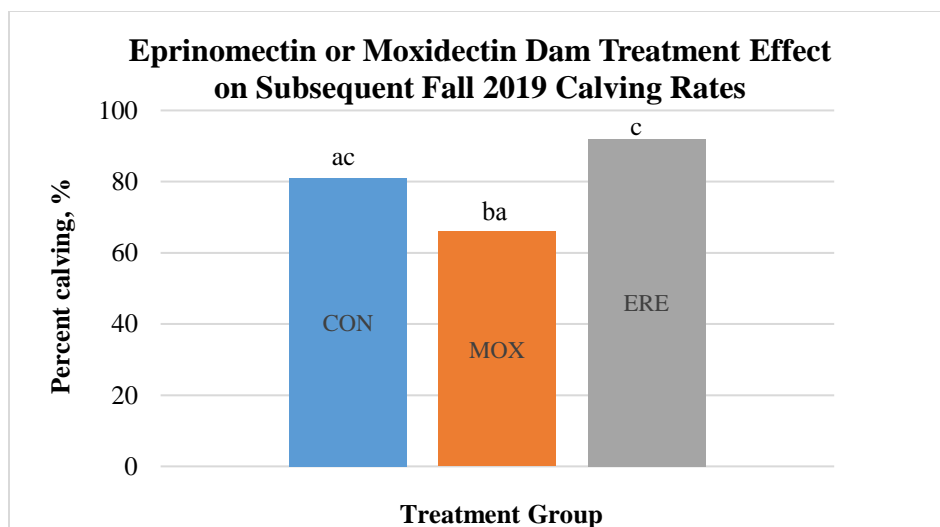


Figure 3. Mean ( $\pm$ SEM) calving rates of fall calving cow treatment groups control, injectable moxidectin (0.2mg/kg of BW) ; injectable extended release eprinomectin (1mg/kg of BW). N=38 CON; 30 MOX; 38 ERE cows per treatment group.

<sup>a-c</sup> Means without common superscripts differ ( $P < 0.05$ )

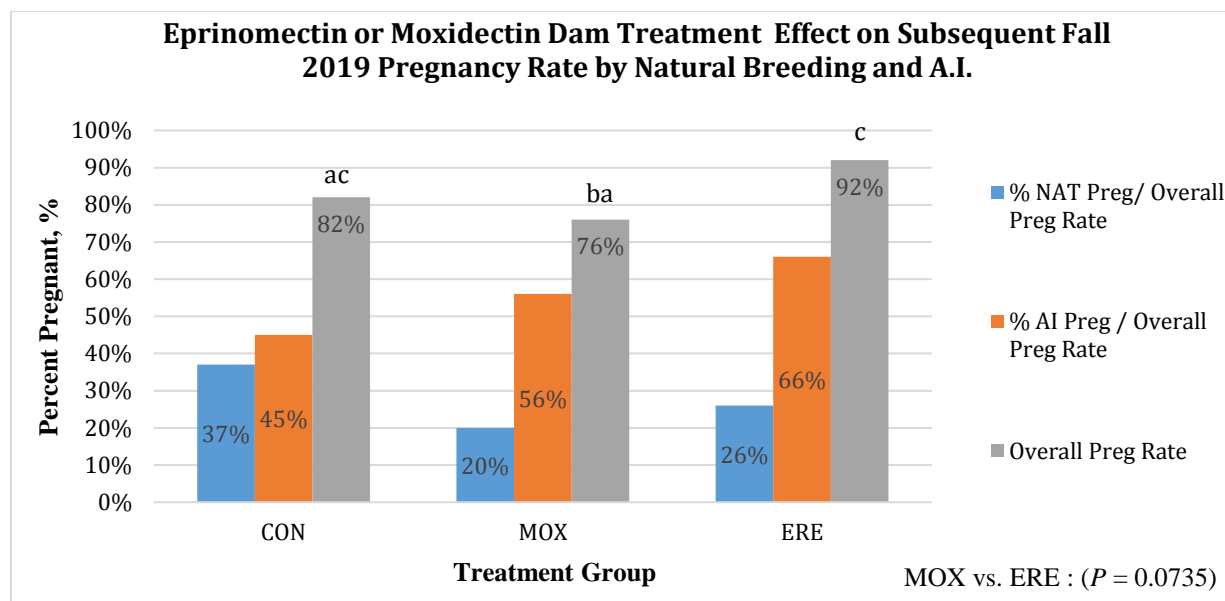


Figure 4. Mean ( $\pm$ SEM) pregnancy rates by natural pregnancy and by artificial insemination of fall calving cow treatment groups control, injectable moxidectin (0.2mg/kg of BW) ; injectable extended release eprinomectin (1mg/kg of BW). N=38 CON; 30 MOX; 38 ERE cows per treatment group.

<sup>a-c</sup>Means without common superscripts tended to differ ( $0.05 < P < 1.0$ )

Table 6. Subsequent (fall 2019) average calving date × dam treatment interaction of multiparous beef cows treated prior to calving in fall 2018 with either Moxidectin or Extended Release Eprinomectin

Item	Treatments <sup>a</sup>			<i>P</i> -Value	CON VS TREATED	MOX VS ERE
	MOX	ERE	CON			
Calving Date	9/16/19	9/20/19	9/23/19	0.23	0.11	0.35

<sup>a</sup>CON= control; MOX= moxidectin; ERE= extended release eprinomectin

\*No significant differences were noted

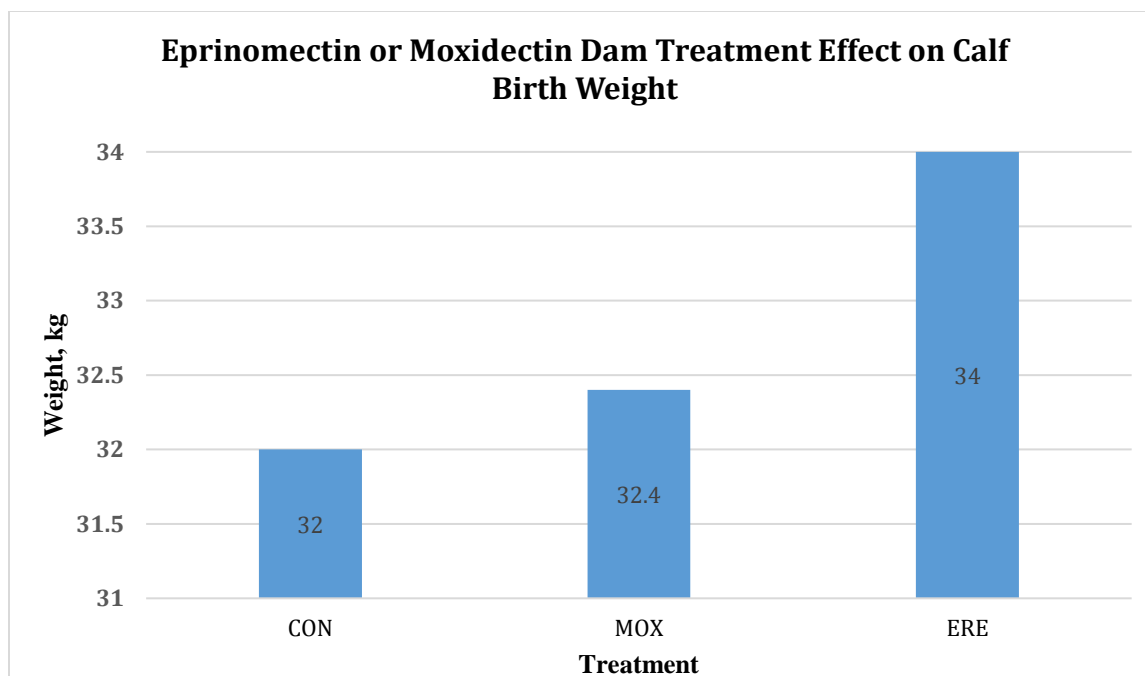


Figure 5. Mean ( $\pm$ SEM) calf birthweight (kg) analyzed by dam treatment. Dam treatments were CON, n=38; injectable moxidectin (0.2mg/kg of BW) MOX, n= 30; injectable extended release eprinomectin (1mg/kg of BW) ERE, n= 38.

\*No significant differences were noted

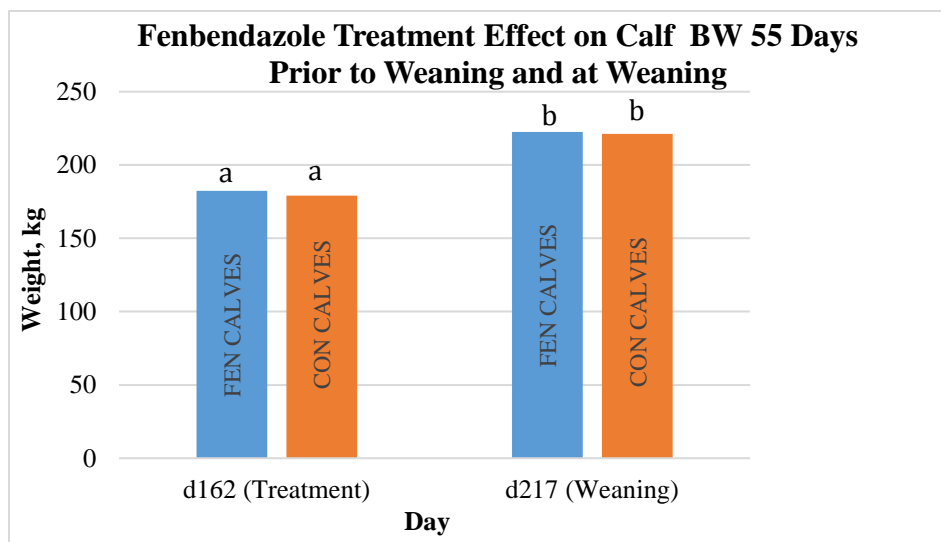


Figure 6. Mean ( $\pm$ SEM) weights (kg) of calf treatment groups: negative control, CON (n = 53) and oral drench fenbendazole (5mg/kg of BW), FEN (n = 53) recorded on d162 and d217 of the study.

<sup>a,b</sup> Means without common superscript differ ( $P < 0.05$ )

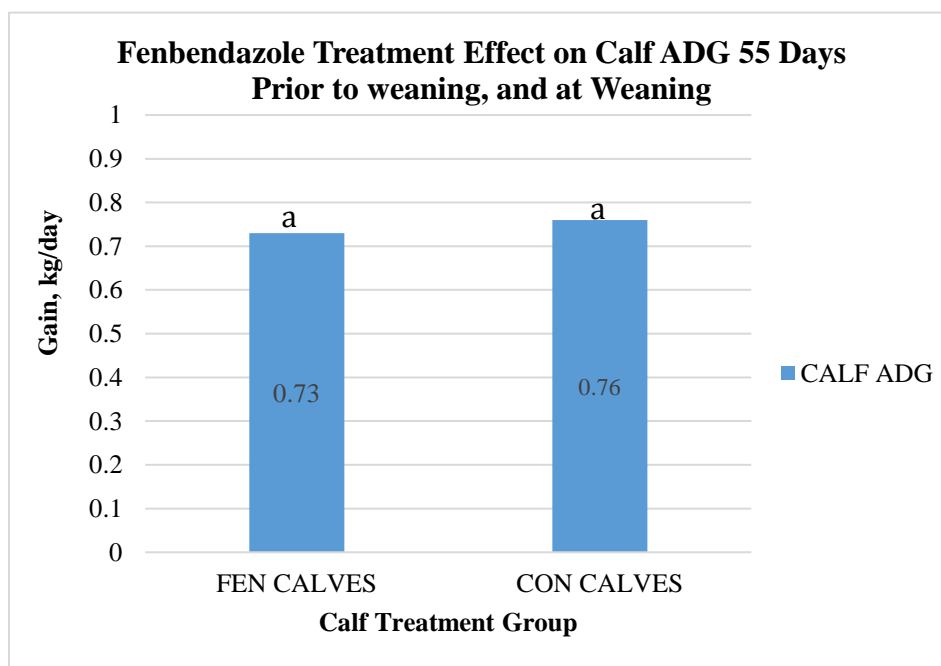


Figure 7. Mean ( $\pm$  SEM) average daily gain (kg/day) of CON (n = 53) and oral drench fenbendazole (5mg/kg of BW) - FEN (n = 53) calves from d162 - d217 of the study.

\*No significant differences were noted

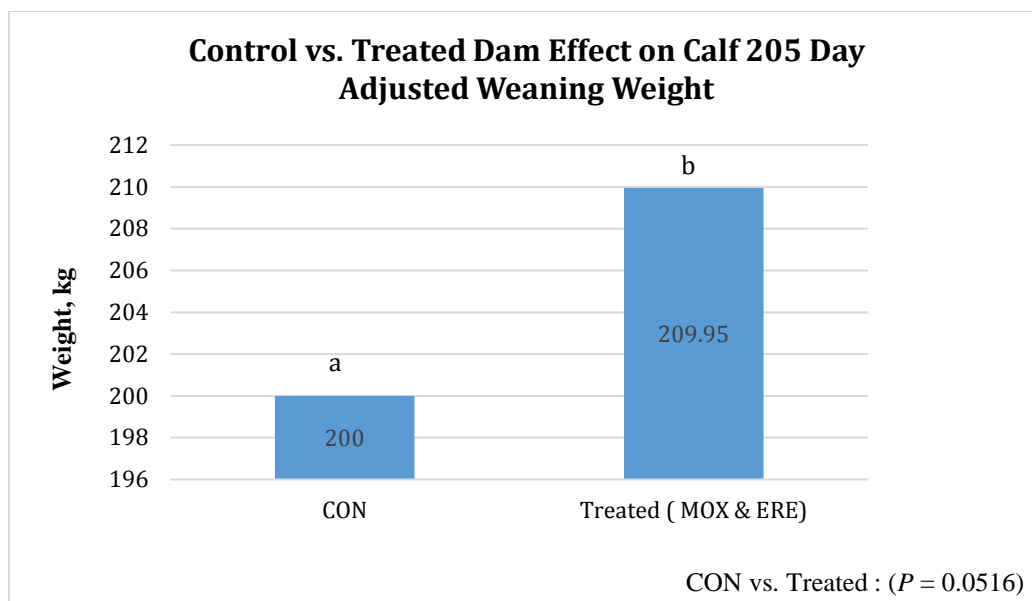


Figure 8. Mean ( $\pm$ SEM) 205 day adjusted weaning weights of calves analyzed by orthogonal contrast of control vs. treated in regards to dam treatment. Dam treatments were CON, n=38; injectable moxidectin (0.2mg/kg of BW) MOX, n= 30; injectable extended release eprinomectin (1mg/kg of BW) ERE, n= 38.

<sup>a,b</sup> Means without common superscripts tended to differ ( $0.05 < P < 0.10$ )

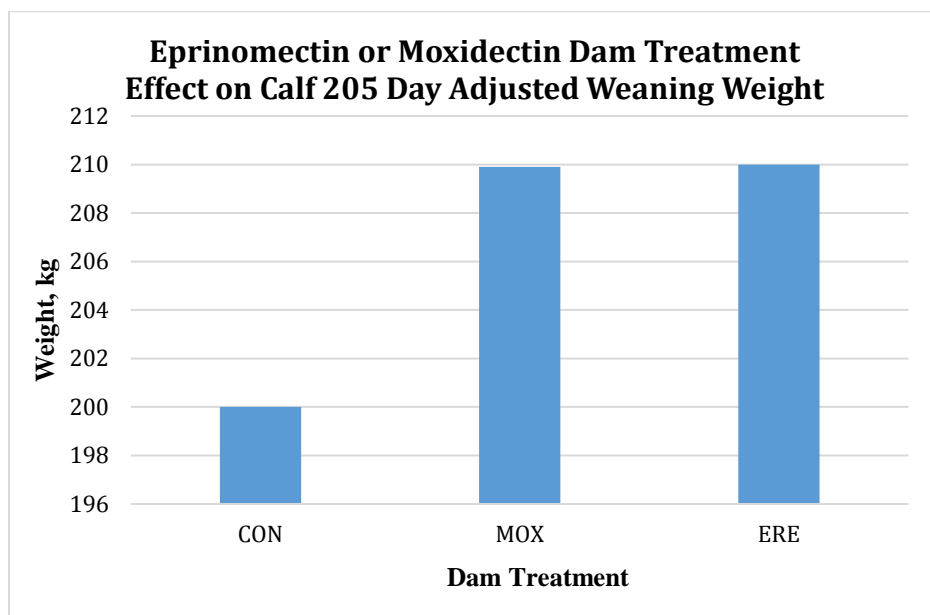


Figure 9. Mean ( $\pm$ SEM) 205 day adjusted weaning weights of calves analyzed by dam treatment. Dam treatments were CON, n=38; injectable moxidectin (0.2mg/kg of BW) MOX, n= 30; injectable extended release eprinomectin (1mg/kg of BW) ERE, n= 38.

\* No significant differences were noted



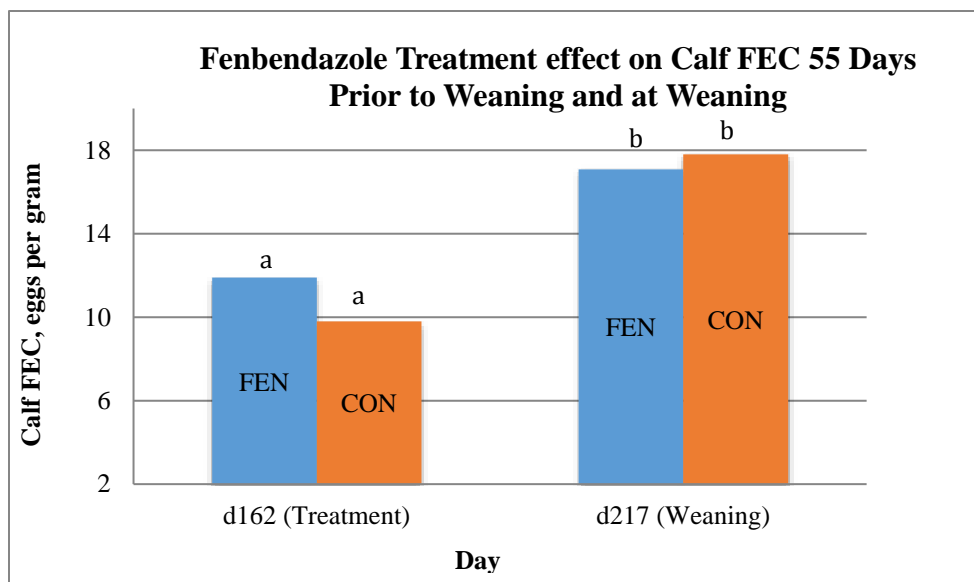


Figure 10. Mean ( $\pm$  SEM) FEC (eggs per gram) from d 162 - d 217 for control (CON), and oral fenbendazole drench (5mg/kg) (FEN) treated calves.

<sup>a,b</sup> Means without common superscripts differ ( $P < 0.05$ )

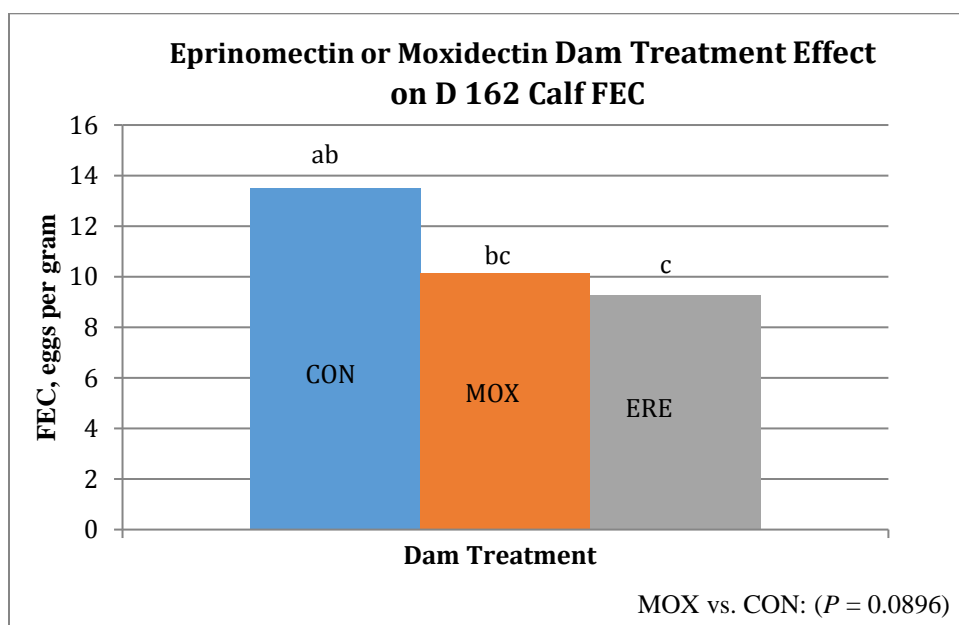


Figure 11. Mean ( $\pm$ SEM) FEC (eggs per gram) of calves on d 162 analyzed by dam treatment interaction. Dam treatments were CON, n=38; injectable moxidectin (0.2mg/kg of BW) MOX, n= 30; injectable extended release eprinomectin (1mg/kg of BW) ERE, n= 38.

<sup>a-c</sup> Means without common superscripts tended to differ ( $0.05 < P < 0.10$ )

## APPENDIX



UNIVERSITY OF  
ARKANSAS

Office of Research Compliance

To: Jeremy Powell  
Fr: Craig Coon  
Date: September 11th, 2018  
Subject: IACUC Approval  
Expiration Date: June 7th, 2019

The Institutional Animal Care and Use Committee (IACUC) has APPROVED your protocol # **19014: *The Efficacy of Eprinomectin LongRange Against Cattle Nematode Parasites and the Effects on Cow/Calf Performance.***

In granting its approval, the IACUC has approved only the information provided. Should there be any further changes to the protocol during the research, please notify the IACUC in writing (via the Modification form) prior to initiating the changes. If the study period is expected to extend beyond June 7th, 2019 you can submit a modification to extend project up to 3 years, or submit a new protocol. By policy the IACUC cannot approve a study for more than 3 years at a time.

The following individuals are approved to work on this study: Jeremy Powell, Tom Yazwinski, Laine Zammit, Toby Lester, Eva Wray, and Reagan Cauble. Please submit personnel additions to this protocol via the modification form prior to their start of work.

The IACUC appreciates your cooperation in complying with University and Federal guidelines involving animal subjects.

CNC/tmp